VENTRICULOPERITONEAL SHUNTS INFECTIONS IN PAEDIATRIC PATIENTS

Dissertation submitted in

Partial fulfillment of the Regulations required for the award of

M.D. DEGREE

In

MICROBIOLOGY– BRANCH IV

The Tamil Nadu

DR. M.G.R. MEDICAL UNIVERSITY

Chennai

MAY 2019.

CERTIFICATE

This is to certify that the enclosed work **"VENTRICULOPERITONEAL SHUNTS INFECTIONS IN PAEDIATRIC PATIENTS"** submitted by **Dr.M.Sangeetha** to The Tamilnadu Dr. MGR Medical University is based on bonafide cases studied and analysed by the candidate in the Department of Microbiology, Coimbatore Medical College Hospital during the period from March 2017 to June 2018 under the guidance and supervision of **Dr.N.Mythily, MD.,** Professor & HOD, Department of Microbiology and the conclusion reached in this study are her own.

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DECLARATION

I, **Dr.M.Sangeetha** solemnly declare that the dissertation entitled **"VENTRICULOPERITONEAL SHUNTS INFECTIONS IN PAEDIATRIC PATIENTS**" was done by me at Coimbatore Medical College Hospital, during the period from July 2017 to June 2018 under the guidance and supervision of **Dr. N. Mythily, M.D.,** Professor & HOD, Department of Microbiology, Coimbatore Medical College, Coimbatore.

This dissertation is submitted to The Tamilnadu Dr. MGR Medical University towards the partial fulfilment of the requirement for the award of M.D. Degree (Branch – IV) in Microbiology.

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Course	:	**MD (Microbiology) Post Graduate**
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College	:	**Coimbatore Medical College & Hospital.**
Dissertation Topic	:	**Ventriculoperitoneal shunts infections in paediatric patients**

The Ethics Committee, Coimbatore Medical College has decided to inform that your Dissertation Proposal is accepted and you are permitted to proceed with the above Study.

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ACKNOWLEDGEMENT

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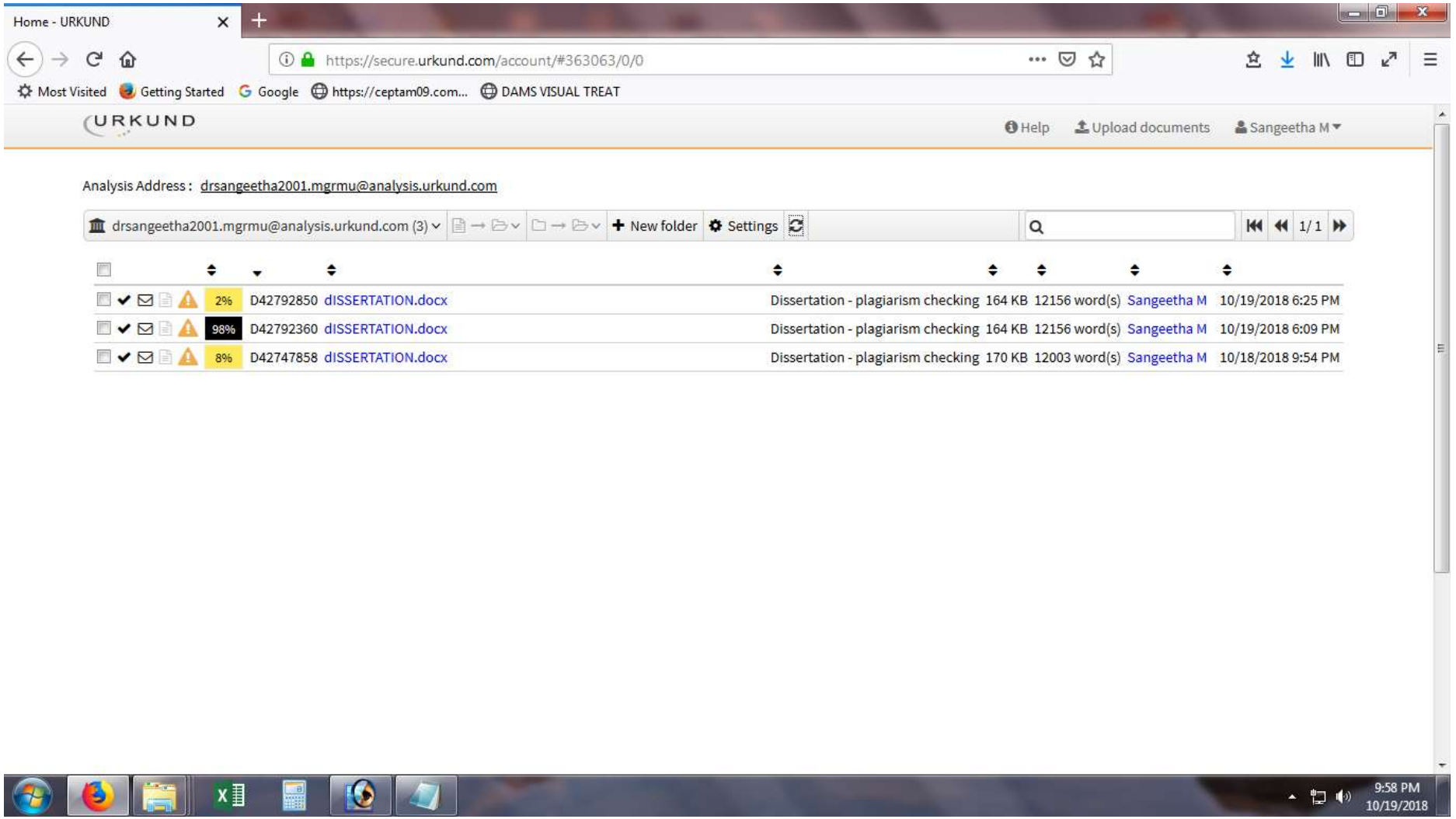
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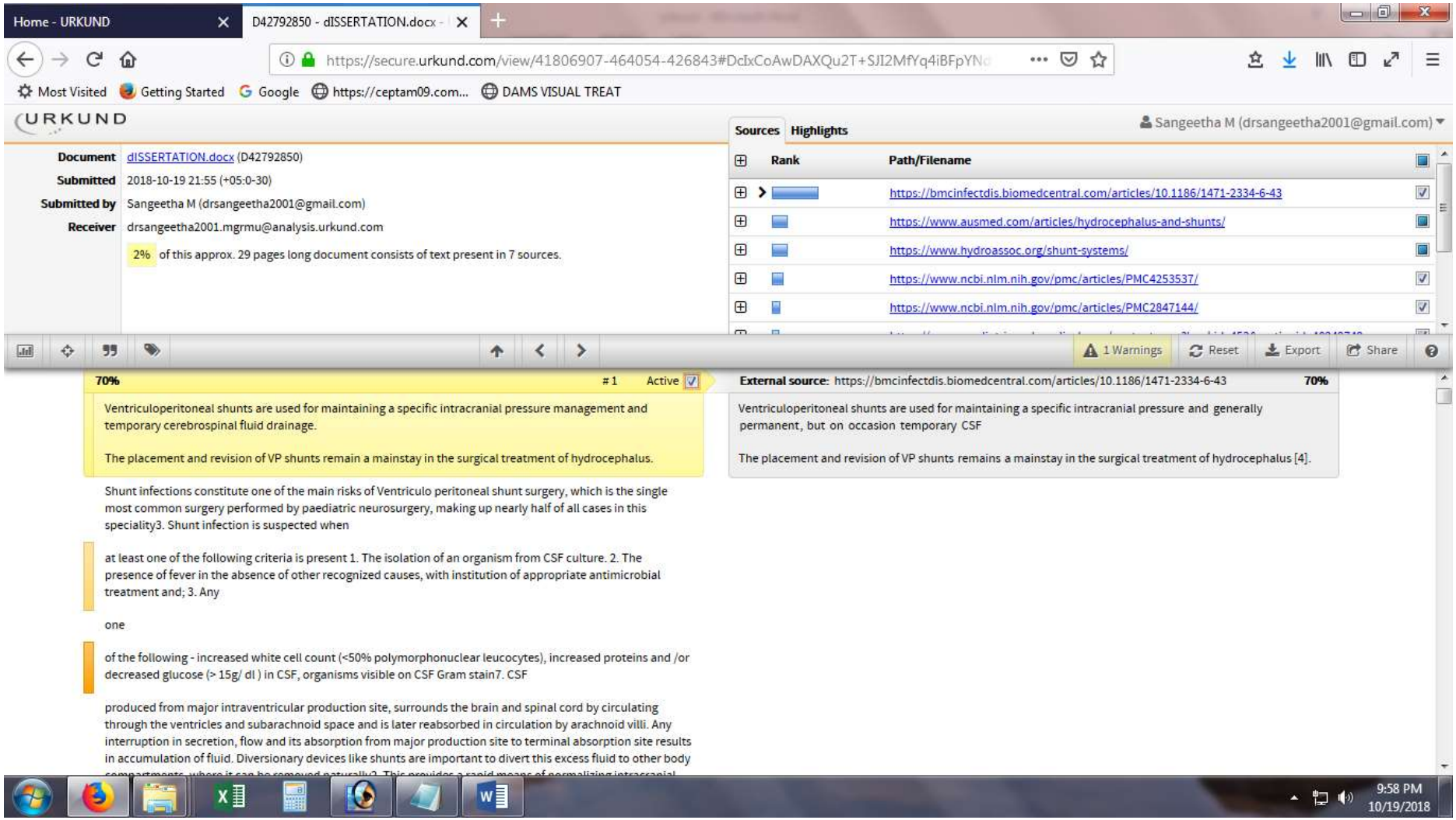
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Ventriculoperitoneal shunts are used for maintaining a specific intracranial pressure management and temporary cerebrospinal fluid drainage.
The placement and revision of VP shunts remain a mainstay in the surgical treatment of hydrocephalus.
Shunt infections constitute one of the main risks of Ventriculo peritoneal shunt surgery, which is the single most common surgery performed by paediatric neurosurgery, making up nearly half of all cases in this speciality3. Shunt infection is suspected when
at least one of the following criteria is present 1. The isolation of an organism from CSF culture. 2. The presence of fever in the absence of other recognized causes, with institution of appropriate antimicrobial treatment and; 3. Any
one
of the following - increased white cell count (<50% polymorphonuclear leucocytes), increased proteins and /or decreased glucose (> 15g/ dl) in CSF, organisms visible on CSF Gram stain7. CSF
produced from major intraventricular production site, surrounds the brain and spinal cord by circulating through the ventricles and subarachnoid space and is later reabsorbed in circulation by arachnoid villi. Any interruption in secretion, flow and its absorption from major production site to terminal absorption site results in accumulation of fluid. Diversionary devices like shunts are important to divert this excess fluid to other body
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Ventriculoperitoneal shunts are used for maintaining a specific intracranial pressure and generally permanent, but on occasion temporary CSF
The placement and revision of VP shunts remains a mainstay in the surgical treatment of hydrocephalus [4].
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This is to certify that this dissertation work titled **"VENTRICULOPERITONEAL SHUNTS INFECTIONS IN PAEDIATRIC PATIENTS"** of the candidate **Dr.M.Sangeetha** with registration Number **201614253** for the award of **Doctor of Medicine** in the branch of **Microbiology**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **2%** percentage of plagiarism in the dissertation.

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ABBREVIATIONS

CLSI	-	Clinical & Laboratory Standards Institute
CONS	-	Coagulase Negative Staphylococci
DDST	-	Double disk diffusion synergy test
ESBL	-	Extended Spectrum ù Lactamases
GNB	-	Gram-negative bacilli
GPC	-	Gram-positive cocci
MBL	-	Metallo ù Lactamases
MIC	-	Minimum Inhibitory Concentration
MRSA	-	Methicillin Resistant *Staphylococcus aureus*
S. aureus	-	*Staphylococcus aureus*
S. epidermidis	-	*Staphylococcus epidermidis*
E.coli	-	*Escherichia coli*
P.aeruginosa	-	*Pseudomonas aeruginosa*
CSF	-	Cerebrospinal Fluid
VP Shunt	-	Ventriculoperitoneal shunts

INTRODUCTION

VENTRICULOPERITONEAL SHUNTS INFECTIONS IN PAEDIATRIC PATIENT

INTRODUCTION

Ventriculoperitoneal shunts are used for maintaining a specific intracranial pressure management and temporary cerebrospinal fluid drainage. The placement and revision of VP shunts remain a mainstay in the surgical treatment of hydrocephalus.

Shunt infections constitute one of the main risks of Ventriculo peritoneal shunt surgery, which is the single most common surgery performed by paediatric neurosurgery, making up nearly half of all cases in this speciality[3].

Shunt infection is suspected when at least one of the following criteria is present

1. The isolation of an organism from CSF culture.
2. The presence of fever in the absence of other recognized causes, with institution of appropriate antimicrobial treatment and;
3. Any one of the following - increased white cell count (>50% polymorphonuclear leucocytes), increased proteins and /or decreased glucose (< 15g/ dl) in CSF, organisms visible on CSF Gram stain[7].

CSF produced from major intraventricular production site, surrounds the brain and spinal cord by circulating through the ventricles and subarachnoid space and is later reabsorbed in circulation by arachnoid villi.

Any interruption in secretion, flow and its absorption from major production site to terminal absorption site results in accumulation of fluid. Diversionary devices like shunts are important to divert this excess fluid to other body compartments, where it can be removed naturally[2]. This provides a rapid means of normalizing intracranial pressure and can prevent neuronal damage and other detrimental sequalae, affecting the milestones and intellectual development of the growing brain[10].

The most common type of shunt is the ventriculo-peritoneal shunt, which drains fluid from the ventricles to the abdomen. Less common types of shunt are;

- Ventriculo-atrial shunts
- Ventriculo- pleural shunts
- Ventriculo-gall bladder shunts

This device has three compartments

1. Ventricular catheter to reach the lateral ventricles of brain.
2. Valve to control the flow.
3. Tubing to divert this excess fluid to peritoneal site.

Though Ventriculo –peritoneal shunt placement is the main stay of hydrocephalus treatment, it is associated with chronic surgical and medical problems. Each revision is associated with malfunction and increases the rate of infection. Incidence of infection ranges from 5-15%. In case of CSF infections due to any device , it is associated with signs and symptoms of acute bacterial meningitis[4].

Infection if untreated causes developmental disorders, mental deficiencies and shortened life expectancy in addition to blindness and other neurological deficits as a result of cerebral injury due to distension of brain tissue[8].

Risk factors include chronological age, gestational age , postconceptional age, sex, birth weight , weight at surgery , indication for shunt placement including myelomeningocele and intra ventricular hemorrhage, trauma , length of hospital stay and post-infective pathology (Tuberculous Menigitis , Pyogenic meningitis, hydrocephalus and sporadic cases)[11].

In patients undergoing a shunt procedure, the infectious pathogen will most likely be a microorganism from the resident bacterial flora of the skin, nasopharynx, and external auditory canal. Prolonged hospital stay is unavoidable and hence nosocomial infections , bacterial coinfections, aspiration of gastric contents in comatose patients, and use of broad spectrum antibiotics are to be considered. Shunt pathogens are Coagulase Negative Staphylococcus (65%) and Staphylococcus aureus which are usually skin commensals, followed by Gram Negative Bacteria (19- 22%), due to bacterial colonization of stomach with aerobes and retrograde infection from peritoneal site as in case of peritonitis[4].

Ventriculoperitoneal infection are classified into two types based on the duration.

Early Shunt Infection - CSF infections within the initial 30 days of ventricular catheter insertion were considered to be early shunt infection. Causative pathogens are Staphylococcus aureus and Coagulase negative Staphylococcus[13].

Late Shunt Infection - CSF infections which occur 30 days after the insertion were considered as late shunt infection. Causative pathogens are Gram negative Bacilli (E.coli, Klebsiella, Citrobacter) and Non fermenters (Pseudomonas and Acinetobacter)[13].

Prior Shunt infections with Staphlococcus aureus causes repeated shunt infections, but in case of coagulase-negative Staphylococcus species infection it is presumably not so.

Recurrence of shunt infection ,means the isolate was different from previous shunt infection. In Relapse of shunt infection the isolate happens to be of the same genus and species and occurs within one month of treatment . A shunt revision was defined as an operative neurosurgical intervention to the CSF shunt[16].

Clinical features includes high/intermittent fever, seizures, vomiting ,increase in head circumference, abdominal distension especially in paediatric cases and a positive CSF analysis as described earlier[19].

Drugs must attain therapeutic concentration in CNS for effective management. Oral drugs with high bioavailability and effective penetration of Blood Brain Barrier can be used in children. Duration of antibiotics administered is usually for 3 to 21 days and CSF culture must be negative

for revision of VP shunt surgeries . Broad spectrum antibiotics are started when signs , symptoms as well as CSF biochemical and cytological reports are supportive of Acute Bacterial Meningitis but culture is the gold standard[20]. Treatment is meticously narrowed down based on CLSI GUIDELINES, to prevent emerging Antibiotic Resistance and to avoid certain drugs to which Intrinsic Resistance is geneticaly transmitted[18].

The low pathogenicity of some implicate pathogens , chronological age of the patient , non specific clinical signs and symptoms , increase in head size with fever [the only symptom below 2 yrs], older children with triad of headache, vomiting and papilloedema make the diagnosis of infection in intact shunt cumbersome. Development of shunt surgeries has remarkably changed the outcome in these patients with vulnerable age group to lead a normal life[20].

VP shunt infection is an important devastating complication of shunt surgery, associated with high morbidity and mortality. In the recent years the organisms associated with these infections are multi drug resistant. Hence early and prompt diagnosis of Ventriculoperitoneal shunt infection is crucial. The study helps to formulate effective antibiotic policy for a better clinical outcome thereby giving a chance to lead a near normal life for these patients[22].

AIM & OBJECTIVES

AIM AND OBJECTIVES

AIM:

To analyse risk factors, microbiological, microbial profile, antibiotic sensitivity and clinical outcome of Ventriculoperitoneal shunt infections in paediatric patients.

OBJECTIVES:

- Analysis of risk factors for developing infections.
- Isolation and identification of pathogens involved.
- To identify resistance pattern among culture positive isolates by antibiotic sensitivity tests.
- Assessment of clinical outcome of post operative VP shunt surgery.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1. CDC 2018 guidelines has provided reporting instructions for CSF shunt infection as SSI-MEN (surgical site infection - meningitis and encephalitis) when infection occurs within 90 days of placement, and if infection occurs beyond 90 days of placement its reported as CNS-MEN (Central Nervous System- meningitis and encephalitis)[14].
2. In case of meningitis (MEN) and encephalitis (IC) present together, it has to be reported as MEN.
3. In case of meningitis (MEN)and brain abscess (IC)present together, it has to be reported as IC and SA if meningitis (MEN) and spinal abscess (SA) are present together.

The principle of ventriculoperitoneal shunts is to drain excess of accumulated cerebrospinal fluid into the peritoneal cavity in case of hydrocephalus thus relieving the pressure in the brain. Development of brain is crucial during the first two years of life, and an indication for ventriculoperitoneal surgery during this age group has both faces of a coin. This common entity in neurology targets the normal hydrodynamics of cerebrospinal fluid surrounding the brain and spinalcord[16].

Hydrocephalus is due to congenital obstruction as in case of aqueduct of Sylvius, congenital malformation like Arnold - Chiari and Dandy-Walker malformation and neural tube defects for which Ventriculoperitoneal shunt insertion is the treatment of choice It has

improved and restored the cognitive and postural equilibrium functions in case of posterior cerebellar tumours. Remarkable increase in survival rate has increase in post traumatic hydrocephalus with subarachnoid haemmorhage and tuberculous meningitis[23].

This meticuolous surgery increases the survival and improves the cognitive memory so that the patient in future can lead an independent life but it's drawbacks vary from life threatening infection to mechanical and biological malfunction.

HISTORICAL REVIEW[17,18,26]

(1621-1675) The understanding of ventricular system and CSF pathway was initiated by Thomas Willis.

(**1876)** Key and Retzeus established the modern concept of CSF circulation.

1881, Carl Wernicke performed the first sterile ventricular puncture and external ventricular drain .

1903, Nicholas Senn performed first recorded surgery using perforated rubber tube, a crude predecessor of the modern ventriculo peritoneal shunt.

1952 , Nulsen and Spitz used rubber shunts to divert CSF, John Holter replaced rubber shunts by silicone shunts and this was used for his hydrocephalic son successfully.

1960, Ransohoff et al proved success rate of 65% with Ventriculo Peritoneal infections.

1970 , peritoneal cavity as best site for CSF diversion was proved by Ames work.

1908 first VP shunt surgery was done by Cushing, but it was instrumental after Scarff's meticuolous work of treating hydrocephalus by ventriculoperitoneal shunts successfully among 55% of 230 patients.

SIGNIFICANCE OF VENTRICULOPERITONEAL SURGERY[27,31,52,53]

- To reduce abnormal intracranial pressure.
- To arrest abnormal activation of inflammatory cytokines in brain parenchyma.

This diligent intervention of ventriculoperitoneal shunt in hydrocephalus is the treatment of choice, because this challenges both cognitive and developmental milestones among children.

INCLUSION CRITERIA FOR VENTRICULOPERITONEAL SHUNT INFECTION

Shunt infection includes both meningitis and encephalitis and must satisfy following criteria;

1) The isolation of an organism from CSF culture or non culture methods

2) Any two clinical signs

1. AGE ≥ 1 YEAR	2. AGE ≤ 1 YEAR
3. Fever or headache	4. Fever, hypothermia, apnea, bradycardia, irritability
5. Meningeal signs	6. Meningeal signs
7. Cranial signs	8. Cranial nerve signs

3 Any one of the supporting documents

a) Increase WBC , elevated protein ,and decreased glucose in CSF

b) Organism visible on Gram stain

c) Organism isolated from blood by culture and non culture methods

d) Diagnostic single antibody titre (Ig M) or four fold increase in paired sera (IgG) for organisms.

INDICATIONS OF INFECTION FOLLOWING VENTRICULOPERITONEAL SHUNT SURGERY.

1) DIAGNOSTIC INDICATIONS

- Suspected cases with signs and symptoms of shunt infection .
- Communicating or Obstructive hydrocephalus.
- Signs in favour of acute bacterial meningitis.
- Signs indicating posterior fossa tumours.
- Congenital causes Meningomyelocele with Arnold Chiari malformations.
- Post – meningitic hydrocephalus
- Signs suggesting CSF leakage or pseudo meningocele.

THERAPEUTIC INDICATIONS[32]

- Malfunction of ventriculoperitoneal shunt device.

CONTRAINDICATIONS

Absolute contraindication include infection over the entry site especially when CSF culture from Extra Ventricular Drain is positive

TYPES OF VENTRICULOPERITONEAL INFECTION[33]

Early onset ventriculoperitoneal infection (SSI-MEN) – (within 90 days of surgical procedure). The predominant causative pathogen are Gram Positive Bacteria associated with increased hospital stay.

Late onset ventriculoperitoneal infection (CNS-MEN) - (after 90 days of Surgical procedure). The predominant causative pathogens are Gram Negative Bacteria associated with multi drug resistance.

Variations in onset of shunt infection & infection rate[34]

In a study conducted by Nebraska university, USA, reported that 90% of infection occurred during first 30 days, with incidence of infection rate from 10 to 20%.

International Surgery Journal published in May 2017 highlights late infection. This study was conducted from 2013 to 2016 with 198 patients, 23 patients had shunt complications within 30 days of shunt surgery and 45 patients had shunt complications within a period of 5 months

EPIDEMOLOGY- global burden[35]

Nearly 200,000 cases occur each year throughout the world and 12,000cases of congenital hydrocephalus in India are reported and awaiting treatment by Ventriculoperitoneal shunt surgery.

The prevalence of hydrocephalus in United States is 0.5% ; Down Syndrome shares the same prevalence as congenital hydrocephalus. This neurosurgical condition treatable by ventriculoperitoeal shunt is more common than spinabifida and CNS tumours in USA[36].

In United States shunt infections account for 2,400 admissions and 59,000 hospital days each year despite aggressive treatment as documented

by HCRN (Hydrocephalus Clinical Research Network) The ratio of shunt revisions to primary shunt placements remain 3: 1 at many health care centres

In India the incidence of congenital hydrocephalus is about(0.2–0.5 /1000) live births according to a study by Advanced Neuroscience Institute, India.

In India, a recent outcome analysis of ventriculoperitoneal shunt surgery in paediatric hydrocephalus from April to June 2018 done at Ashish Hospital and Research Institute, Madhya Pradesh, shows the incidence of overall shunt complications to be 35,76%. Shunt revision accounts for 27%, shunt blocade 45.94% ,shunt infection was 16.21% and shunt migration was 10.81%[37].

Prospective study to formulate a strategy to prevent infections was done among 486 cases admitted during the period from 2006 to 2013 in the Institute of Neurology, Madras Medical College[38]. In accordance with other studies where infection rate was 3.8 to 27%, the Institute documented 5.4% as infection rate .Multiple revisions in this study are associated with infection rate ranging from 5.4% to 14.28%. one of the reason for multiple revisions are associated with increased cellular content of CSF seen in post tuberculous meningitis[39].

ISK FACTORS [40,41]

Dr.Simon's studies has postulated the risk factors for surgeries in his publication which was supported by PCMC innovative research

grant. In his retrospective cohort study of children from 0 to 18 years on association of intraventricular hemorrhage secondary to prematurity, he has enumerated the following as risk factors:

1) PATIENT FACTORS

- Sex of the baby - (male preponderance)
- Low Birth Weight babies
- Preterm babies
- Age of the baby
- Weight of baby at the time of surgery.
- LOS preceding shunt surgeries

Patient factors are related to immaturity of the neonatal immune system, poor skin barrier protection , and altered skin bacterial density according to studies by Pople, Bayston and Hayward[50].

2) SURGEON FACTORS

- Experience of neuro surgeon
- Use of neuroendoscope.

3) MEDICAL DECISIONS

- Use of prophylactic IV antibiotics
- Use of prophylacticintrathecal antibiotic use.

4) SURGICAL DECISIONS

- Shunt valve brand
- Antibiotic impregnated shunt tubing

- Distal shunt location
- Case priority
- Case duration

IMMUNOPATHOGENESIS :

MISINTERPRETATION OF DEFENCES IN THE CNS -

Infection of CNS is recognized by microglia and astrocytes. Microglia activation after identifying the pathogen results in secretion of TNF –α , IL - 1 β , nitric oxide and super oxide free radicals, thus displaying bactericidal activity against parenchymal brain infection[30.31,32].

Microglial production of IL-10 is neuro protective and strengthens neuronal synapse formation. These unique protective factors are harvested as therapeutic targets to narrow down the infection. Astrocytes show protective effect by expressing pattern recognition receptors and produce chemokines and cytokines in response to infectious stimuli . Normal CNS homeostatic functions are maintained by Astrocytes against both Gram Negative Citrobacter meningitis and Staphylococcus aureus parenchymal CNS infection. Astrocytes prevent infection by their control of gap junction communications and production of proinflammatory mediators[42].

Inflammation of brain parenchymal cells and misinterpretation against host cell mediated immunity results in IQ loss and increased risk of seizures in CNS infections[43].

DEVICE ASSOCIATED INFECTIONS

SHUNT HARDWARE INFECTIONS

External shunt infections constitute only 5% of shunt infections Internal shunt infections are due to colonization of the inner surfaces of the shunt tubing and valve. The organism exist in biofilm state raising its minimal inhibitory concentration 500 times more than in vitro sensitivity result[44].

IDSA International Disease Society of America recommends removal of the device followed by Extra Ventricular Drain[45]. Sterility of CSF is required before insertion of new shunt to prevent recurrence of infection with standard protocol .

BIOFILMS

Phenol soluble molecules (PSN) molecules have a role in structure and development of biofilms. These molecules lyse WBC and RBC, and thereby inhibit immune function. They are produced by staphyloccal strains .

Staphyloccal species has a wide range of toxins which disrupts innate immune system affecting leukocidin A and B. This is sufficient to kill macrophages, dendritic cells and neutrophils . Pore forming toxins are Alpha- toxin and Valentine leukocidin (PVL) which have been reported in community acquired methicillin resistant strains[46].

PARTS OF VP SHUNT

- **INFLOW CATHETER – VENTRICULAR CATHETER**

This portion of VP Shunt drains the CSF from the ventricles or sub arachnoid space and leaves the brain through a small hole in the Skull, which then runs under the skin[47].

- **VALVE MECHANISM**

Value mechanism regulates the differential pressure or controls the flow through the shunt tubing. This portion serves to connect the inflow catheter that lies between the skin and the skull, usually behind the ear.

Different types of value mechanism are;

- Fixed differential pressure valves
- Fixed differential pressure valves with an antisiphon mechanism
- Programmable differential valves - most preferred valves
- Programmable differential valves with an antisiphon mechanism

- **OUT FLOW CATHETER - DISTAL CATHETER**

This runs under the skin and directs CSF from the valve to the abdominal cavity . Minimal access to infection because its the longest and largest component of ventriculo peritoneal shunt. Barium Impregnation allows radiographic visualization of accurate anatomical position of outflow catheter[48].

Different types of VP Shunt[49]

1) **Spitz -Holter valve** - unidirectional valve currently used in tertiary care units.
2) **Ommaya valves** with reservoirs to allow easy access for ventricular sampling and easy access of drugs .
3) Inbuilt **pressure sensing valves**

INVESTIGATIONS – IMAGING TECHNIQUES CONFIRM THE DIAGNOSIS

- **MRI** - Establishes the anatomy and pathology of infection.
- **CT** - Follow up of patients with prior shunt infection

  To decide in critical care of undiagnosed patients.

  - **Post Obstructive Hydrocephalus[10,11,17]** - Dilation of lateral ventricles and obstruction of fourth ventricle.
  - **Tuberculous meningitis** - prominent lepto meningeal and basal cistern enlargement.
- **USG** - Cranial ultrasound for periventricular hyper echogenicity and GV IVH
  - germinal matrix intra ventricular haemorrhage (GV IVH) in premature infants.,
  - infants with myelomeningocele

MICROBIOLOGY OF CAUSATIVE PATHOGEN

Whenever possible adequate sample collection and immediate processing is important for better recovery of implicated pathogen as a complex polymicrobial condition is involved[52].

Proximal part of shunt infections causes meningitis or ventriculitis, distal part of shunt infections causes fever , anorexia , abdominal distension and acute abdomen[53].

Pathology in colonization causes Gram Positive Organisms to predominate in early onset infections. Staphylococcus and Coagulase Negative Staphylococcus are isolated following infections from upper respiratory illness or following transient bacteremic attack among individuals at risk[54].

Gram Negative Bacteria has been reported recently in tertiary care units. Post –meningitis brain abscess due to citrobacter in neonates, and coliforms with infection of terminal end of shunt device and gastric perforation, has been documented in a study by Kumar et al[5],.

Stamos , Kaufman and Yogev in their study (Ventriculoperitoneal shunt infections with Gram Negative Bacteria) suggested that GNB infections accounts for 7-24% in all Ventriculoperitoneal cases[56]. Common nosocomial pathogens involved are Enterobacteriaceae and Non Fermenters, Pseudomonas aeruginosa 25%, E.coli 20%, Acinetobacter are 15%. Predictors of GNB are related to intraperitoneal inflammation, hematogenous spread and bowel perforation of distal tip of VP catheter tip.

The major concern of Gram Negative Coliforms are increase in antimicrobial resistance by various mechanisms by extended spectrum β- lactamase or AmpC enzymes. In case of Gram Positive Organism , methicillin -resistant Staphylococcus aureus (MRSA) and Vancomycin Resistant Enterococci (VRE) are to be considered[57].

RESISTANCE OF PRIORITY PATHOGENS

Injudicious use of antibiotics have resulted in the emergence of antibiotic resistant strains. Hence identification of the species and their resistant pattern is important in the treatment of such infections[58].

The increase in the rates of antibiotic resistance is a major concern in both non-fermenting bacilli and members of the Enterobacteriaceae family. Antimicrobial resistance in addition hampers the effectiveness of treatment and thus the patient remains infectious for a long time thereby increasing the spread of resistant microorganisms to others[59].

In February 2017 **WHO** published a list of Antibiotic resistant "**Priority Pathogens**" requiring newer antimicrobials, which is classified into critical, high, and medium priority pathogens.[44]

Critical pathogens requiring newer antibiotics include Pseudomonas, Acinetobacter, Enterobacteriaceae (Proteus, Klebsiella, E.coli, Serratia). These bacteria are resistant to number of antibiotics including Penicillin's, III generation Cephalosporins&Carbapenems, which is the best available antibiotic for treating them[60].

LIST OF "WHO" PRIORITY PATHOGENS REQUIRING NEWER ANTIBIOTICS :

Priority I : Critical

1. Acinetobacter -carbapenem resistant.
2. Pseudomonas -carbapenem resistant.
3. Enterobacteriaceae (Proteus, Klebsiella, E.coli, Serratia) - carbapenem resistant, ESBL producing.

The global spread of Carbapenemase - producing Gram-negative pathogens is of special concern in healthcare and community settings. Carbapenemase confers resistance to most beta-lactam antibiotics including penicillin, cephalosporins and carbapenems. Carbapenems have emerged as the agent of choice for managing Enterobacteriaceae, as they are resistant to aminoglycosides, fluoroquinolones, Penicillin and third generation cephalosporins[61].

Nosocomial isolates of S. aureus, Enterococcus species, E.coli, Klebsiella, Pseudomonas, & Acinetobacter, have become multi drug resistant, extremely drug resistant and pan-drug resistant, producing beta-lactamases including ESBL, MBL & Amp - C. Metallo-β-lactamases (MBL), has the ability to hydrolyse Penicillins, Cephalosporins, and Carbapenems.

Phenotypic methods includes combined disk diffusion test, double diffusion test, modified Hodge's test and Epsilometer strip test to identify the Carbapenemase production . Molecular characterization by PCR is the

only available tool for MDR, XDR, and PDR strains, based on Carbapenemase encoding genes.[8] PCR, used to identify the genes[62].

Early detection of infection is critical in paediatric neurosurgery , for adhering to strict infection control practices, formulating an effective antibiotic policy to prevent the spread of these MBL producing strains, and treatment with alternative higher antimicrobial agents.

Clinical Infectious Disease (2017) suggest that incidence of A.baumannii resistant strains are increasing across the globe because of its tendency to develop pan drug resistance (PDR). PDR is defined as when an isolate exhibit resistance toall seven. Anti-pseudomonal agents which includes Anti-pseudomonal penicillins, cephalosporins, carbapenems, monobactems, quinolones, aminoglycosides and polymyxins[63].

I. SHUNT COMPLICATIONS

1) Mechanical Complications

- Mechanical failure and infection contribute to 90% of complications
- Infection
- Shunt blockages(proximal ,valve or distal)
- Fracture or disconnection
- Migration
- Over drainage

2) Biological Complications

- ❖ Isolation (trapping) of ventricles
- ❖ Malposition
- ❖ Intracranial haemorrhage
- ❖ Viscus perforation

II.SHUNT BLOCKAGE

Shunt obstruction is absolute indication for shunt revision. In the majority ,it is due to blockage of ventricular catheter by cellular debris, choroid plexus and brain tissue[64].

III. THE SLIT VENTRICLE SYNDROME

Slit ventricle syndrome is a rare symptomatic condition presenting with neuro imaging of small ventricles in a patient with venticulo peritoneal shunt and its misinterpretation as a properly working shunt[65].

IV. ABDOMINAL COMPLICATIONS

Viscus perforation is a result of complication of the initial insertion or as result of chronic erosion of the catheter tip through the viscus wall. Signs of peritoneal sepsis or occasional extrusion of the catheter tip at the anus, umbilicus or vagina[66].

V. INTRA ABDOMINAL FLUID COLLECTION[67,68,69]

Abdominal pain and distension are the common symptoms .Localized collection of CSF within peritoneal cavity is common. Ultrasound findings are confirmatory .

CLINICAL FEATURES SUPPORTING SHUNT INFECTION

The clinical features of shunt infection are variable, depending on the pathogenesis of infection, virulence of organism and type of shunt.

The most common symptoms are headache , nausea, lethargy and changes in mental status (seen in about 65% of infected patients) which occur in shunt malfunction secondary to the infection[70].

Fever is reported in 20 – 90% cases, and absence of fever does not exclude infection of ventriculo peritoneal shunt.

Symptoms and signs are referable to the proximal or distal portion of the shunt. Infection arising in the proximal portion of the shunt causes meningitis or ventriculitis in about 30% of cases with resultant shunt obstruction or decreased function[71].

Symptoms referable to the distal portion may be due to peritonitis such as fever, anorexia, abdominal distension and other signs of acute abdomen. Low virulence organisms present few signs such as abdominal tenderness and guarding .Fluid collections occur due to encystment of the shunt catheter tip. The deposited CSF is not absorbed causing loculation of pockets of fluid within the abdomen resulting in partial or complete shunt obstruction with shunt extrusion when Gram Negative Bacteria is associated.

DIAGNOSIS OF SHUNT INFECTION

The diagnosis of CSF shunt infections is made by culture of the shunt reservoir fluid or CSF or blood sample before administration of antibiotics.. Blood culture is also of limited value in ventriculoperitoneal shunt infection but it is positive in up to 90% of vascular shunts[72].

The CSF sample is subjected to cell count including differential count, biochemical analysis (CSF glucose and protein), gram stain and culture[73].

High white blood cell counts reflect infection, but infection may be present even with normal cell counts. Normally the CSF has less than 5 leukocytes per ml.

In case of tuberculous meningitis , gross appearance of CSF may present with fibrin web and predominant mononuclear cells more than 100-1000 cells /mm3.

CSF eosinophil count can be elevated and has been found to be associated with indolent infection. Cell counts can undergo alteration by recent surgery due to inflammatory response or due to spilled blood.

The CSF glucose levels may be reduced and protein levels elevated. Glucose levels may be in the normal range in most cases and not very useful.

Gram staining helps in denoting the type of causative micro organism, but absence of bacterial morphotypes does not exclude the infection. CSF culture from the shunt or reservoir is the most valuable in establishing the

diagnosis of infection.Cultures are usually positive even in absence of CSF pleocytosis or abnormal biochemical parameters[76].

Cultures may require several days of incubation before being discarded as negative. A positive culture indicates true infection. In patients with external ventricular drain, CSF pleocytosis and a positive culture (obtained from the ventricular catheter) indicates definite infection.

Absence of a positive gram stain of CSF culture and a progressive decrease in CSF glucose and increase in CSF protein with advancing pleocytosis indicates a suspected infection[77].

Patients with distal occlusion of VP shunt and shunt extrusion presents as acute abdomen and they must undergo revision surgeries. A CT or ultrasound scan of the abdomen identifies CSF loculations at the terminus. Peritoneal symptoms clear within 12 hours after removal of an infected distal catheter.

FACTORS TO BE CONSIDERED IN THE THERAPY OF AN INFECTED CSF SHUNT INCLUDE :

1. Selection of antimicrobial therapy
2. Timing of hardware removal
3. Timing of shunt replacement
4. Duration of antimicrobial therapy

ANTIMICROBIAL THERAPY& MANAGEMENT OF DRUG RESISTANCE [78,79]

The antimicrobial agent of choice must have greater distribution of bactericidal activity in central nervous system which includes Ampicillin, Ceftriaxone, and Meropenem . Frequently used aminoglycoside (Gentamycin) and Nucleic acid synthesis inhibitor (Ciprofloxacin) does not attain therapeutic concentration in CSF according to Principles of Antimicrobial action and resistance by [Bailey & Scott 14th edition].Minimum Inhibitory Concentration of Carbapenems is effective method to prevent anti microbial resistance.

Direct instillation of antimicrobial agents into the ventricles and use of antibiotic impregnated shunts reduce the biofilm formation by skin commensals and help in better outcome of results to both the patient and tertiary care centre[12].

SHUNT REMOVAL AND REPLACEMENT[55]

A new shunt is usually not placed until CSF culture is negative for bacterial growth. The recommend interval between shunt revision and reinsertion is approximately 10 -14 days with atleast 48 hours between the final negative CSF culture and reinsertion.

A variety of methods are used to support shunt deprived patients that include shunt exteriorization, placement of external ventricular drain or lumbar drainage catheters.

Ventriculitis of shunt infection clear more quickly with external drainage, the treatment success usually greater than 85% . The greatest risk of the EVD is secondary infection..

SHUNT REINSERTION[62]

Shunt infections caused by CoNS with normal CSF findings, and negative cultures for 48 hours after externalization indicates absence of infection and patient can be reshunted on the third day after removal.

If CoNS was isolated with abnormal CSF biochemistry and pleocytosis, 7 days of antimicrobial therapy is recommended and repeat CSF culture is advised before reshunting.

For shunt infections caused by S.aureus or gram negative bacilli , 10 days of antimicrobial therapy is followed in tertiary care centres. Repeat CSF negative culture is recommended before reshunting.

Infections with Gram Negative Organism are difficult to treat because of resistance offered and ability to cause reinfection. Focus of infection must be identified which may take its orgin in gastric fluid, peritoneum, or intestines[38].

Intravenous antibiotic treatment usually results in rapid bacteriological clearance with resolution of the CSF pleocytosis if standard protocols are followed.

PREVENTION

Meta – analyses have concluded that prophylactic antibiotics can reduce of infection by about 50%.Antibiotic impregnated catheters for EVD and CSF shunts have been shown to reduce colonization and infection of the catheter with gram – positive organism[37].

Expanded poly-tetra-fluro-ethylene VP shunt is alternative to silicone VP shunts. Newer advancements are Poly Hydroxyl Ethyl Metha Acrylate (p HEMA) and Poly-Vinyl Pyrrolidone for surface functionalization. Radio opaque indicators, typically utilizing Barium sulfate or tantalum are incorporated for better clinical outcome.

MATERIALS & METHODS

MATERIALS AND METHODS

Places of study:

The study of " Ventriculoperitoneal shunt infections in paediatric patients" was conducted in the Department of Microbiology, Coimbatore Medical College Hospital among 60 paediatric cases. CSF, shunt tip and blood samples were collected in Neurosurgical Operation Theatres from children with signs and symptoms of infection following the first ventriculoperitoneal shunt surgery in post operative period . Extraventricular drain was established and samples were collected for microbiological, biochemical and cytological analysis to document the etiological agents of Ventriculoperitoneal shunt infections.

Study Period:

The study was conducted for a period of one year from March 2017 to June 2018.

Type of Study: Prospective study

Approval from the ethical committee was obtained prior to the conduct of the study.

Ethical clearance:

As this study involved the collection of clinical samples from paediatric patients in Operation Theatres, ethical clearance was obtained before the commencement of the study.

Informed consent:

Informed consent was obtained from all parents whose children were involved in the study. A filled in proforma was obtained from parents of paediatric patients with the details including Name, Age, Sex, Ward, Clinical Diagnosis, Risk factors, Antenatal, Natal, Post-natal, history & age of insertion of first and subsequent ventriculoperitoneal shunts with follow up.

Sample

In the present study CSF sample , blood sample , shunt tip samples from 60 paediatric patients who have undergone ventriculoperitoneal shunt surgery due to prematurity , anatomical defect, infective pathology, post traumatic hydrocephalus and hydrocephalus following posterior fossa tumours were obtained.

Inclusion Criteria

Paediatric patients who have undergone ventriculoperitoneal shunt surgeries with following criteria were included in the study:

1) Signs and symptoms suggestive of acute bacterial meningitis
2) Shunt obstruction
3) Shunt malfunction

ExclusionCriteria

1. Patients who have skin infections.
2. Patients with focal sepsis and terminating illness.
3. Immunocompromised patients with hydrocephalus

4. Patients who have no signs and symptoms of infection after surgery.
5. Adults above 13 yrs

COLLECTION AND TRANSPORT OF SAMPLES :

The samples were collected from Neuro Surgery Operation Theatre of both Elective and Emergency posted cases. Samples were transported to Microbiology department and processed without delay.

SAMPLE COLLECTION :

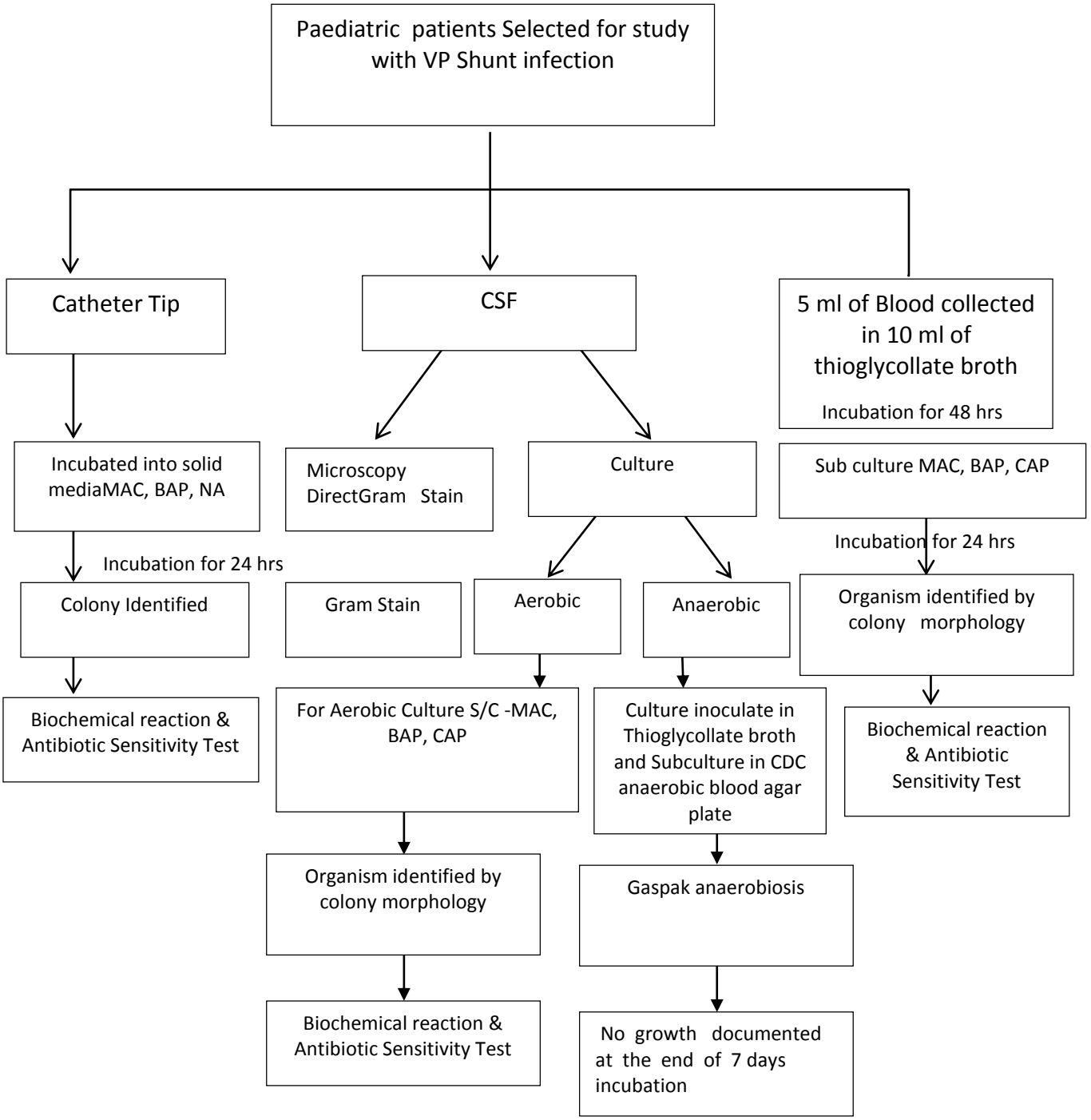
- Autoclaved screw caped container for CSF sample. – SAMPLE 1
- Autoclaved screw caped container for CSF shunt tip _ SAMPLE 2
- 2ml blood sample in 10 ml of Thioglycollate broth _ SAMPLE 3

PROCESSING OF SAMPLES INCLUDES

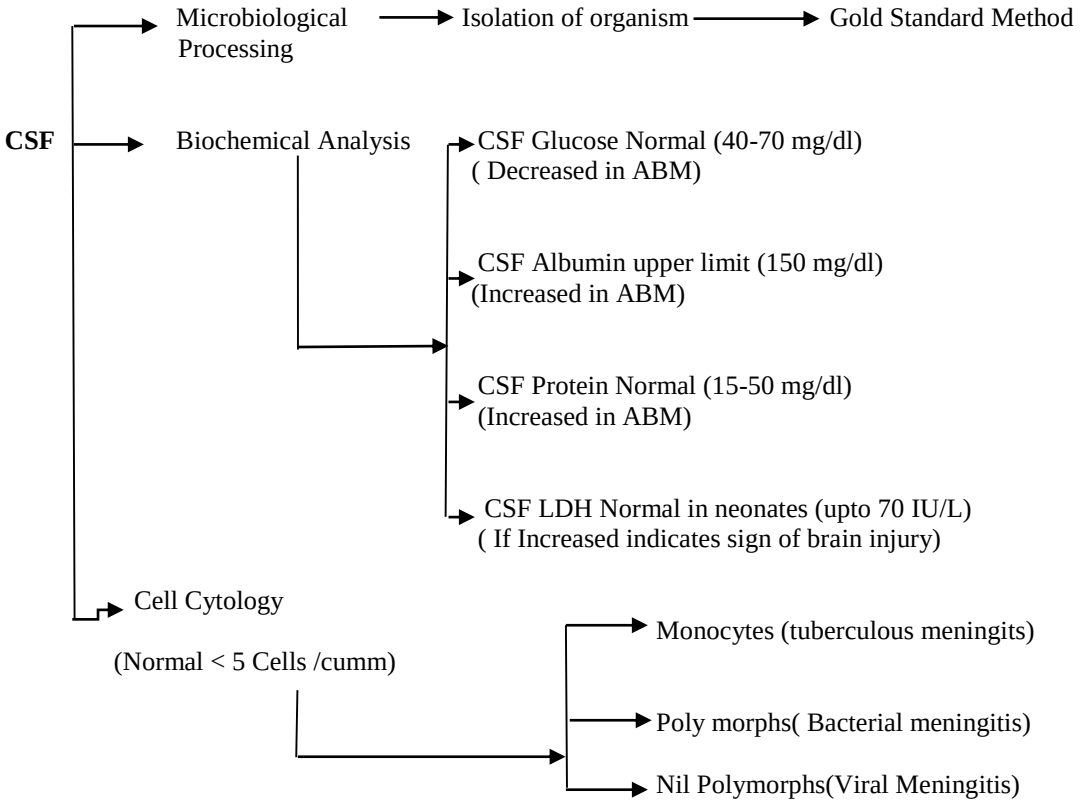
- MICROBIOLOGICAL PROCESSING OF SAMPLE 1,2,3.
- BIOCHEMICAL ANALYSIS OF CSF
- CELL CYTOLOGY STUDY OF CSF

MICROBIOLOGICAL PROCESSING

❖ PROTOCOL FOLLOWED:



MULTIVARIATE ANALYSIS OF SAMPLES IN THIS STUDY



CSF:

MACROSCOPY EXAMINATION :

1) Naked eye examination of CSF to observe if clear, turbid, purulent, blood stained, cobweb appearance is present or absent.

2) In case of centrifuged CSF samples the deposit provides better information of pus cells and bacteria for screening with microscope.

MICROSCOPIC EXAMINATION :

CSF samples may have scanty cells and bacteria , hence a thick smear or a heap-up technique with oval marking on under surface of slide is done and heat fixed .Gram stain is performed by Hucker method

and observation is under 100X . In case of purulent CSF, thin smear is done for better interpretation and heat fixed followed by Gram staining. The smear is heat fixed with methanol so that it provides relevant information for documentation in future.

On day 2 if there is evidence of growth it must be followed by (Hanging drop) motility test. Few colonies are taken from culture enriched in peptone water for 20 minutes and then Hanging drop method is performed to clearly delineate motile and non motile bacteria. The edge of drop is seen under 10X and the edge is carefully turned to high power 40X to observe for motility.

CONVENTIONAL CULTURE METHODS FOR AEROBIC CULTURE:

1)CSF and shunt sample for recovery of fastidious organisms, were inoculated into Chocolate agar, Mac Conkey agar and Blood agar plates and incubated for 37C in 5-10% carbon dioxide in a candle jar for 18 to 72 hrs.

2)For recovery of Non fastidious organisms , CSF and shunt tip samples were inoculated into Nutrient agar plate and MacConkey agar plate.

3)Colony morphology was studied with Gram's stain and motility of the organism was confirmed on second day. Isolated growth of

colonies were subjected to biochemical reactions and antibiotic sensitivity test.

4)Shunt tips were processed by rolling the tip over the surface of media and transferred the shunt tip to Brain Heart Infusion broth by using sterile forceps.

5)1 to 2 ml of blood is collected in 10 ml of Thioglycollate broth and subcultured after 48 hrs in BAP, CAP and Mac Conkey agar plate.

PROCESSING AND FURTHER IDENTIFICATION OF ANAEROBIC BACTERIA :

PRINCIPLE :

Anaerobiosis is created by displacing oxygen from the jar by chemical methods. In this method a sachet containing sodium bicarbonate and sodium borohydride which react chemically in presence of water ,to produce hydrogen and carbondioxide is used.

Anaerobic culture of Cerebrospinal fluid is done with CSF sample enriched in thioglycollate broth for 48 hrs, later subcultured on CDC Anaerobic Blood agar plate by streak culture method and placed in Gaspak anaerobic jar. Pseudomonas aeruginosa ATCCC 27853 which is a obligate aerobe is used as a biological indicator and methylene blue as a chemical indicator is used to check the effectiveness of anaerobiosis.

The plates are observed for the colony characteristics, hemolysis and pigmentation at regular intervals. If no growth is observed at the end of 24 hrs continued incubation for 48 hrs and extend upto seven days. Isolation of growth is confirmed with Gram stained smear from colonies to identify obligate anaerobes.

No anaerobic were isolated from any of the samples.

BIOCHEMICAL REACTIONS:

As per NCCLS guidelines the following biochemical reactions are done.

BIOCHEMICAL REACTIONS		
Reactions in favour of Gram Positive Organisms	**Reactions in favour of both GPC & GNB**	**Reaction in favour of GramNegative Organisms**
➢ Coagulase test	➢ Catalase test ➢ Urease test ➢ VogesProskauer test ➢ Hugh Leifson's(OF) test	➢ Indole test ➢ Citrate ➢ Triple sugar ion ➢ Methyl red ➢ Decarboxylase ➢ Nitrate test ➢ Fermentation test ➢ MMM test

COAGULASE TEST -

Purpose of this test-

1) To test the unique property of clotting of plasma by Staphylococcus aureus which secretes coagulase enzyme .

2) **Definitive test** for Staphylococcus aureus and it contributes for virulence.

It differentiates S.aureus from Coagulase Negative Staphylococci. Slide coagulase test and Tube Coagulase test are two methods involed in this test.

a) **SLIDE COAGULASE TEST**

This test detects the presence of bound coagulase . Suspected growth of white opaque colonies are to be emulsified in sterile saline to form a milky suspension on a clean glass slide . A drop of citrated plasma is added to milky suspension and observed for visible clumps within 10 secs. Control is made with Staphylococcus aureus ATCC 25923 to avoid false positive results.

b) TUBE COAGULASE TEST

This test detects the presence of free coagulase . To 0.5ml of overnight broth pure culture of Staphylococcus add 0.5ml of fresh plasma incubated in a waterbath at 37^0C . Every 30 minutes , the test tube is tilted and observe for clot formation upto 4hrs. Positive controls are kept. Readings are observed at end of second and fourth hour respectively. Formation of a firm clot is positive for enzyme coagulase

CATALASE TEST: (Tube method).

Purpose of this test- 1)To prevent accumulation of Hydrogen peroxide and catalyse the reaction so that it converts this lethal reagent into water and oxygen.

2) Differentiate members of Micrococcaceae from members of Streptococcaceae.

Procedure

1) Slide method

2) Tube method.

Few individual colonies to be tested were picked up by a sterile glass rod and introduced into sterile glass test tube containing 3% hydrogen peroxide. production of immediate brisk effervescence within 30 seconds indicates catalase production

OXIDASE TEST (Wet filter paper method):

Purpose of this test - All enterobacteriaceae are oxidase negative.

Procedure

WET FILTER PAPER METHOD -

Freshly prepared reagent is used in this test .Oxidase reagent (tetra methyl p-phenylene diamine dihydrochloride) was placed in a petri dish and the colony to be tested was smeared on the filter paper. If it turns into deep purple in 10 seconds the organism is oxidase positive.

INDOLE:

Purpose of this test - 1) Ability of organism to split tryptophan.

This test demonstrates the production of indole by spliting tryptophan into indole and pyruvic acid. 2 ml of 24-48 hour broth culture was taken in a test tube and to this 0.5ml Kovac's reagent was added gently along the sides. Formation of a red colour ring at the junction was taken as a positive test.

CITRATE UTILIZATION TEST:

Purpose of this test - Citrate is used as sole source of carbon.

The organisms were streaked on the surface of a slant of Simmon's citrate medium and incubated at 37ºC for 18-24 hours. Development of deep blue colour of the medium indicates presence of growth and its taken as citrate positive.

UREASE TEST:

Purpose of this test - Ability of organism to split urease enzyme

The organism was streaked on the slope of Christensen's urease medium and incubated at 37ºC for 18-24 hours. Urease positive cultures produced a pink colour.

METHYL RED TEST:

Purpose of this test - Quantitative test for detection of acid production.

A pure culture of the test organism was inoculated into 5 ml of glucose phosphate broth and incubated for 48-72 hours at 35°C. To this

5 drops of methyl red reagent was added. The development of bright red colour indicates a positive test.

VOGES-PROSKAUER TEST:

Purpose of this test - To identify those bacteria that produce acetoin as chief end product of glucose fermentation

Glucose phosphate broth (5 ml) was inoculated with a pure culture of the test organism and incubated at 35°C for 24 hours and to this 0.6 ml of 5% alpha naphthol followed by 0.2ml of 40% KOH was added and shaken gently. Acetoin formation was indicated by the appearance of eosin pink colour in 10 minute

TRIPLE SUGAR IRON AGAR MEDIUM (TSI):

The composite solid agar medium contains 3 sugars glucose, lactose and sucrose. The medium was distributed in tubes with a butt and slant . Using a straight wire, the organism from primary isolation plate was stabbed into the butt and streaked on the slant. TSI was incubated for 18-24 hours at 37ºC, and observed for the presence of growth and fermentation. Phenol red is used as indicator of acid production and Ferric salts as an indicator of hydrogen sulphide production.

Interpretation:

Acid (A) / Acid (A): Glucose, lactose & sucrose fermented which is characteristic of lactose fermenting bacteria such as E.coli & Klebsiella, with or without production of gas .

Alkaline(K) / No change (NC) : No fermentation of carbohydrates, characteristic of non fermenting bacteria such as Pseudomonas & Acinetobacter.

Alkaline(K) / Acid(A) with H2S & Gas : Non Lactose fermenters showed alkaline slant, and fermentation of butt, with production of abundant H_2S & gas production . This is typical of Proteus and Salmonella paratyphi B infection.

DECARBOXYLASE & DIHYDROLASE TEST:

Purpose of this test – It measures the enzymatic ability of an organism to decarboxylate an amino acid to form amines.

Few isolated colonies from the nutrient agar plate were inoculated in 4 tubes of Moller`s decarboxylase medium containing lysine, ornithine and arginine hydrochloride and control. Sterile mineral oil was overlaid on the surface of the tubes and incubated at 35°C for 18-24 hours. Purple colour change indicates that the test was positive.

OXIDATION FERMENTATION TEST (HUGH AND LEIFSON's)

Purpose of this test -This test is used to differentiate between oxidation and fermentative reaction.

Two tubes containing OF medium were inoculated heavily with the isolated colonies using a sterile loop. One tube was covered with a 1 cm layer of sterile mineral oil and other tube remained open. Both tubes were incubated at 35°c in ambient air and examined daily for 2-3 days.

CARBOHYDRATE FERMENTATION TESTS:

Purpose of this test- It detects ability of organism to ferment specific sugar incorporated into the medium with production of acid with or without gas.

Sugars like 1% glucose, 1% sucrose, 1% lactose, 1% maltose and 1% mannose were tested individually for oxidative utilization. The medium turns yellow with acid production by bacteria**.**

MANNITOL MOTILITY TEST:

Purpose of this test - To demonstrate the motility of organism.

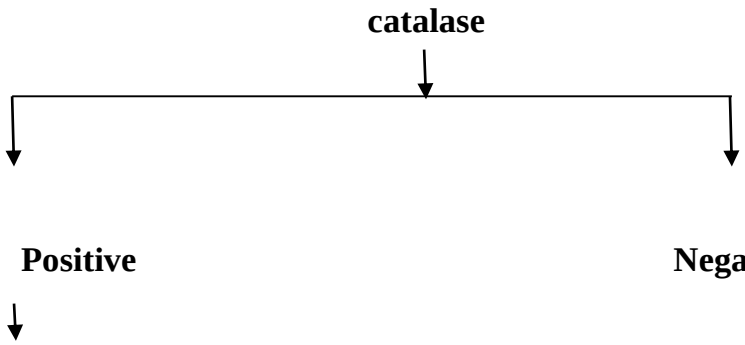
A pure colony was picked using a straight wire and stabbed in the middle of about half the depth of the mannitol motility medium and incubated for 18- 24 hours at 35°C.

Interpretation:

Motile: Diffuse zone of growth flaring out from the streak line .

Non motile: organisms were confined to the line of inoculation

Processsing of Gram –positive cocci in clusters



i) *Staphylococcus species* *Streptococcus species*

ii) *Micrococcus species* *Stomatococcus species*

Staphylococcus species

1. Modified oxidase – *(Negative*)
2. Furazolidone 100µg – (*sensitive)*
3. Bacitracin 0.04 U – (Resistant)
4. Modified Hugh- Leifson

O/F test – fermentative

Micrococcus species

1. Modified oxidsase – (*Positive)*
2. Furazolidone 100µg – *(Resistant*)
3. Bacitracin 0.04 U – (sensitive)
4. Modified Hugh- Leifson

O/F test-oxidativ

A battery of Biochemical reactions to identify various species of CoNS were put up and identification done as follows.

properties	S aureus	S epidermidis	S. haemolyticus	S .lugdunensis
Pigmentation	present	absent	variable	variable
Bound coagulase	+	-	-	-
Tube coagulase	+	_	_	slow
Ornithine decarboxylase	-	-	-	+
Mannitol to acid	+	_	+	_
Urease test	hydrolysed	-	hydrolysed	-
Trehalose to acid	+	_	+	+

DETECTION OF ANTIMICROBIAL SUSCEPTIBILITY PATTERN:

Antimicrobial susceptibility was done in Muller - Hinton Agar plate by Kirby -Bauer Disc diffusion method with test inoculum 0.5 McFarland lawn culture. and overnight incubation with the following ATCC control strains.

ATCC CONTROL STRAINS:

Staph aureus -ATCC 25923

E.coli - ATCC 25922

Pseudomonas – ATCC 27853

Antibiotic panel for Gram Positive Organism

The antibiotics used for Gram Positive Cocci were Penicillin (10 U), Cefoxitin (30 mcg), Trimethoprim-sulfamethoxazole (1.25/23.75 mcg), Linezolid (30 mg), Amikacin (30 mcg) , MIC for Vancomycin and Colistin

Antibiotic panel for Lactose fermenter :

The antibiotics used for Gram-Negative Bacilli were Ampicillin (10 mcg), P ipracillin/tazobactam (100/10 mcg), Ceftazidime (30 mcg), Ceftriaxone (30 mcg), Cefepime (30 mcg), Ceftazidime / clavulanic acid (75/30 mcg), Amikacin (30 mcg), Gentamicin (10 mcg), Netilmicin (30 mcg), Imipenem (10 mcg), Meropenem (10 mcg), Aztreonam (30 mcg), Polymyxin B (300 mcg), Colistin (10 mcg), Trimethoprim sulfamethaxazole (1.25/23.75 mcg**).**

Antibiotic panel for Non-Lactose Fermenter :

Antibiotics used for Pseudomonas aeruginosa were Piperacillin (100 mcg), Piperacillin/tazobactam (100/10 mcg), Ceftazidime (30 mcg), Cefepime (30 mcg), Amikacin (10 mcg), Gentamicin (10 mcg), Imipenem (10 mcg), Meropenem (10 mcg), Netilmicin (30 mcg), Aztreonam (30 mcg), Polymyxin B (300 mcg), Colistin (10 mcg).

ANTIBIOTIC SUSCEPTIBILITY TESTING:

This test was done by modified Kirby-Bauer disc diffusion technique using Mueller Hinton agar. A single colony of the test organism was taken from the plate with a wire loop, and was inoculated into peptone water and

incubated for 18- 24 hrs at 37ºC. The result was matched with 0.5 McFarland turbidity standard.

Preparation of 0.5 McFarland standards

1. Prepare 1% w/v solution of Sulphuric acid by adding 1ml of concentrated sulphuric acid to 99 ml of water. Mix well.
2. Prepare 1% w/v solution of barium chloride by dissolving 0.5g of dehydrated barium chloride in 50ml of distilled water.

This can be stored at room temperature for up to six months. The 0.5 McFarland standard provides an optical density equivalent to the density of 1.5×10^8 colony forming units/ml.

AST by Kirby- Bauer method:

1) Mueller-Hinton agar was prepared according to the manufacturer's instructions and poured into 9cm diameter petri dishes to a depth of 4mm.

2) **Antibiotic Discs** were stored in a tightly sealed container with desiccant at 2ºc to 8ºc. Before opening the container, discs were allowed to equilibrate to room temperature for one to two hours to minimize condensation and to reduce the possibility of moisture affecting the concentration of antimicrobial agents

3) All the isolates were tested for Antibiotic susceptibility pattern, based on CLSI guidelines.

Test to report [Pencillinase –Labile Pencillins] - (CLSI-2018)

Penicillins should be used to test the susceptibility of all staphylococcus. Penicillin discs 10units are placed on the MHA agar plate, and observed after overnight incubation. Zone size of more than 29mm is considered to be sensitive and zone size less than 28 is Resistant.

Test to report Pencillinase –Stable Pencillins - (CLSI-2018)

Cefoxitin is tested as a surrogate marker for oxacillin. The test is done with 30mcg cefoxitin disk , the zone size of more than 22mm is considerd to be sensitive and when its less than 21mm its considered to be resistant for Staph aureus.

In case of CONS, the sensitive zone must be more than 25mm and less than 24mm is considered as resistant.

E strips for detecting MIC for Vancomycin :

MIC tests by E strips were done to determine the susceptibility of all isolates of Staphylococcus to Vancomycin, for Gram Positive Organisms.

For S.aureus $\leq$ 2mg/mL was considered to be sensitive and $\geq$ 16mg/mL was considered to be resistant.

For CoNS $\leq$ 4mg/mL was considered to be sensitive and $\geq$32mg/mL to be considered to be resistant.

GRAM NEGATIVE ORGANISMS:

EXTENDED SPECTRUM β LACTAMASE (ESBL) DETECTION :

1) SCREENING METHODS- STANDARD DISC DIFFUSION PROCEDURE

Isolates of gram negative bacilli showing the following resistance pattern were taken to be ESBL producing strains.

Antibiotic zone diameter for possible ESBL producing strains:

- Cefpodoxime (10µg)) ≤ 17mm
- Ceftazidime(30µ g) ≤ 22mm
- Cefotaxime(30µ g) ≤ 27mm
- Ceftriaxone(30µ g) ≤ 25mm
- Aztreonam(30µ g) ≤ 27mm

2) CONFIRMATORY TEST -STANDARD DISC DIFFUSION PROCEDURE

With a sterile bacteriological loop, 3-5 identical colonies were picked from culture grown overnight and inoculated into 5 ml of nutrient broth. The broth was incubated at 35º C for 2-4 hrs and turbidity matched with 0.5 McFarland standard . Lawn culture of the test organism was made on MHA plate . Antibiotic discs 1) Ceftazidime (CAZ 30µg) and Ceftazidime with clavunate (CAC 30µg/ 10µg) 2) Cefotaxime (CTX 30µg) and Cefotaxime with clavunate (CEC 30µg/ 10µg) were placed on the plate and incubated at

37ºC overnight. An increase in zone diameter of 5mm or more for Ceftazidime with Clavunate and Cefotaxime with Clavunate than their corresponding cephalosporin is confirmatory.

4) **ESBL DETECTION STRIP METHOD**

The ESBL detection strip is coated with Ceftazidime , Cefotaxime and Cefepime on the upper half and lower half has the above drugs with clavulanic acid and tazobactam mixture in a concentration gradient. 3 to 5 colonies of overnight culture of the organism is transferred to a BHI broth and turbidity matched to 0.5 McFarland standard. The suspension is streaked on a MHA plate with a sterile swab and a Ezy MIC strip is placed on it with an applicator and incubated. The value of MIC is read where the ellipse intersects the scale on the strip .

DETERMINATION OF MIC FOR MEROPENEM AND COLISTIN BY EPSILOMETER OR E –STRIP METHOD.

E strip is a Quantitative method of detecting MIC by applying principles of both dilution and diffusion of antibiotic into the medium. E-strips of Colistin and Meropenem which contain predefined gradient of antibiotic concentration immobilised in its length. Following incubation of the test organism, an elliptical zone of inhibition is produced surrounding the strip. The antibiotic concentration at which the ellipse edge intersects the strip gives the Minimal Inhibitory Concentration of the drug.

PHENOTYPIC METHODS TO DETECT METALLO -BETA-LACTAMASES:

1. **IMIPENEM AND IMIPENEM EDTA COMBINED DISC TEST(CDT)**:
2. **MEROPENEM- EDTA DOUBLE DISC SYNERGY TEST(DDST)**:
3. **MBL E TEST:**

1) IMIPENEM AND .IMIPENEM-EDTA COMBINED DISC TEST (CDT):

The 0.5M EDTA solution was prepared by dissolving 18.61 g of EDTA in 100ml of distilled water and pH was adjusted to 8 using sodium hydroxide. The prepared solution was sterilized by autoclaving. The test organism was inoculated on to Mueller Hinton agar according to the CLSI guidelines. Then two Imipenem discs (Hi Media) each of 10µg concentration were placed 15-20mm apart on the plate and appropriately 10 µL of EDTA solution were added to one imipenem disc with the help of a micropipette to obtain the desired concentration of 750µg. The plates were incubated for 16 to 18 hours at 37°C and the inhibition zones of the combined disc and Imipenem disc alone were compared.

In this test, if there is ≥ 7mm increase in the zone of inhibition around Imipenem EDTA combined disc than Imipenem disc alone, then the test is positive. It indicates that the test organism produces Metallo-beta-lactamase enzymes.

II.MEROPENEM- EDTA DOUBLE DISC SYNERGY TEST(DD

The organisms to be tested were inoculated on to the Mueller Hinton agar plate as per the CLSI guidelines . A 10µg Meropenem disc was placed on the MHA plate at a distance of 20 mm centre to centre from the EDTA disc (with 10µL of 0.5M EDTA to get the required 750µg concentration). The MHA plate is then incubated at 37◦C for a duration of about 16-18 hours. If there was enhancement in the inhibition zone of > 5 mm in the EDTA disc than the Meropenem disc the test is positive. The test organism is identified as a Metallo-beta-lactamase producer.

3) MBL E TEST

MBL E test strip is a unique strip for the phenotypic detection of MBL & is coated with mixture of Meropenem + EDTA and Meropenem in a concentration gradient manner. The strip is made of porous material and the antibiotics are distributed evenly on either side of the strip. It was used to determine the minimum inhibitory concentration of the drug for the test strain. E test MBL strip has a double sided antibiotic concentration in a range of Meropenem (MP) 0.125 to 8 µg/ml and Meropenem + EDTA (MPI) 0.032 to 2 µg/ml with a fixed concentration of EDTA.

Procedure:

The inoculum was prepared with 4-5 colonies from 24 hr young broth culture and inoculated as a lawn culture on Muller Hinton agar after adjusting the turbidity to 0.5 Mc Far land standards. The MBL E test strip container was taken from the freezer and kept at room temperature for 15 minutes before opening. The strip was then taken with a sterile forceps or E test applicator and applied to the dried agar surface with the MIC scale facing upwards. The plate was incubated aerobically for 16-18 hrs at 37^0C.

Interpretation:

The MIC of the isolate was read where the zone of inhibition intersects the strip. The MIC for MP/MPI $\geq$ 8 or formation of an ellipse was considered positive for MBL production.

Fig 1: Ventriculoperitoneal Shunt placement in a one year baby

Fig 2: Ventriculoperitoneal shunt tube

Fig 3: Infected ventricular and peritoneal catheter tips in BHI broth

Fig 4: Direct Gram stain of CSF showing pus cells and GPC

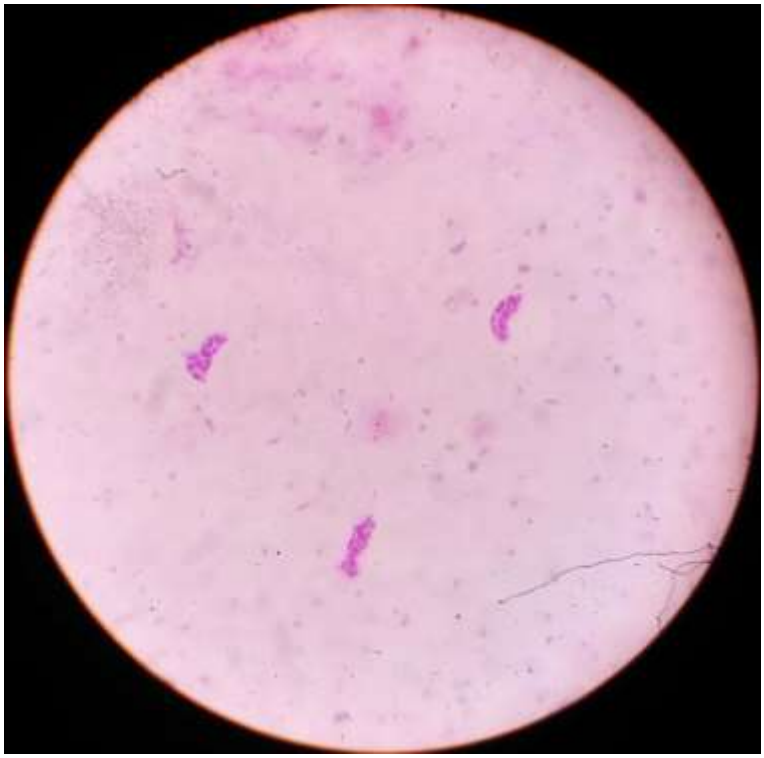


Fig 5: Direct Gram stain of CSF showing pus cells and Gram Negative Bacilli

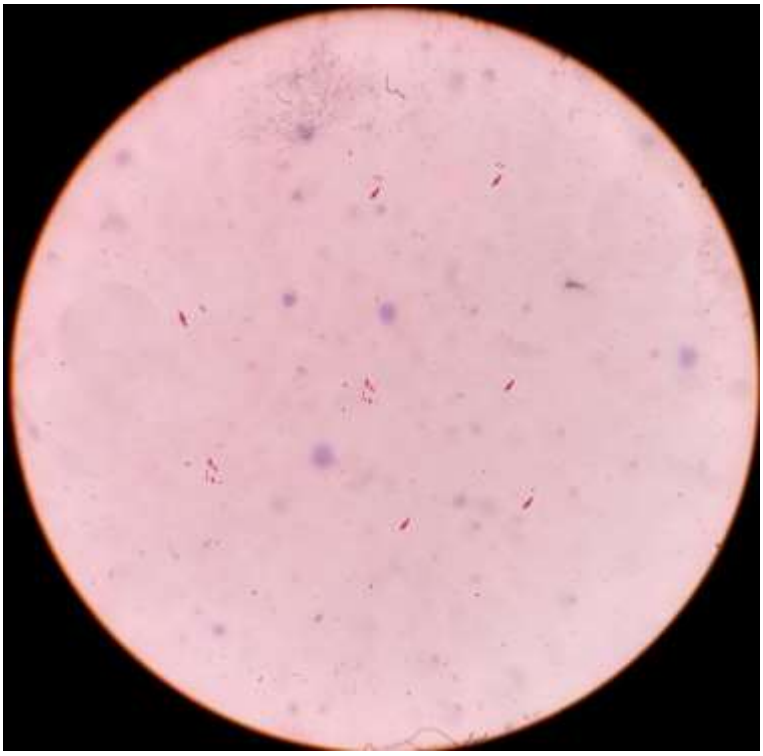


Fig 6: Beta hemolytic colonies of Staphylococcus aureus in 5% sheep blood agar

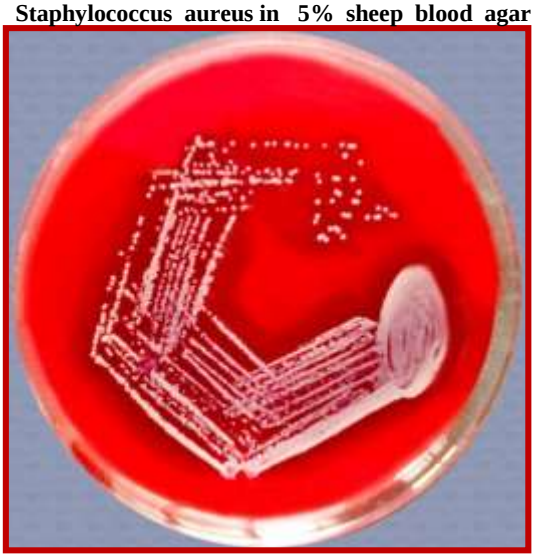


Fig 7: Tube coagulase test of *Staphylococcus aureus*

Fig 8: A. Mannitol non fermenting colonies of CoNS
B. Mannitol fermenting colonies of staph aureus

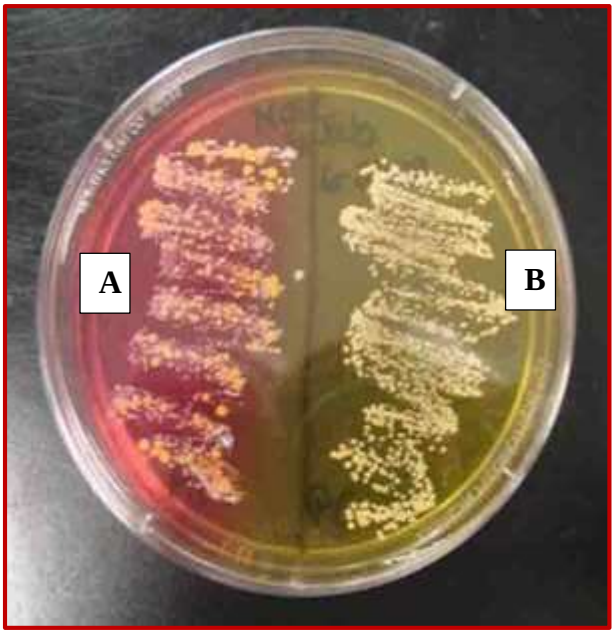


***Fig 9: Escherichia coli* on McConkey Agar**

Fig 10: Pigment producing Pseudomonas on Nutrient agar plate

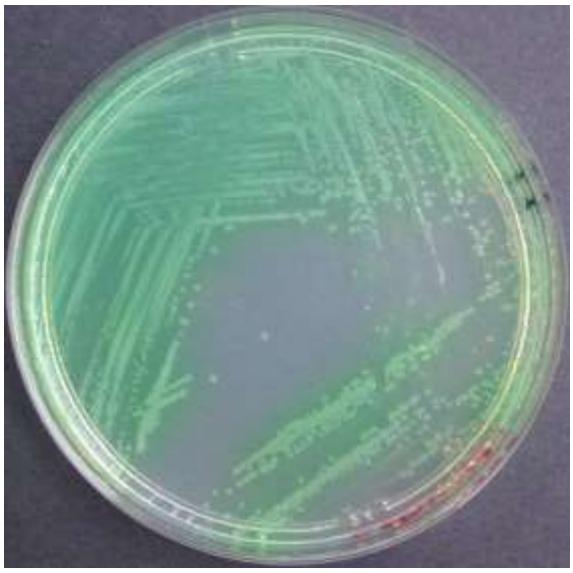


Fig 11: Pale lactose fermenting colonies of Acinetobacter

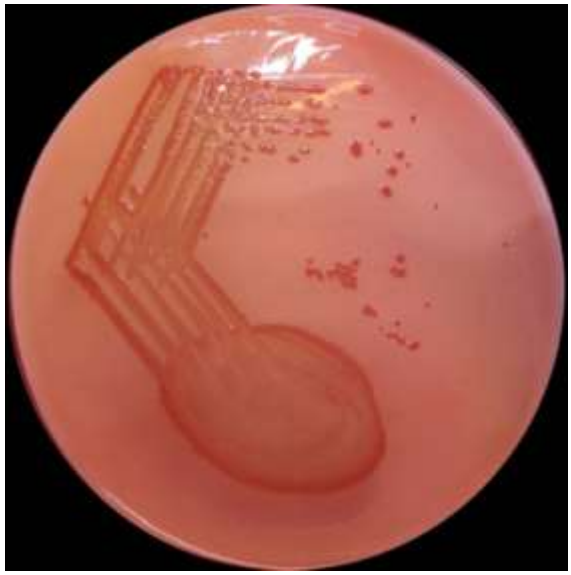


Figure 12: Antibiotic Sensitivity of Staphylococcus aureus (CX – Resistant) by disc diffusion method

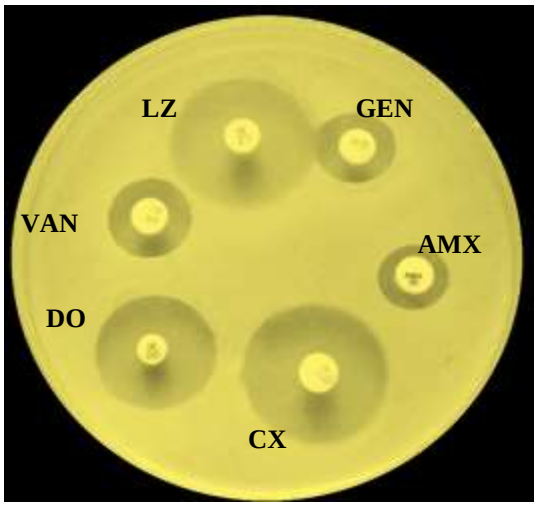


Fig 13: AST by Kirby – Bauer Method (Mueller Hinton Agar) Resistant to Meropenem

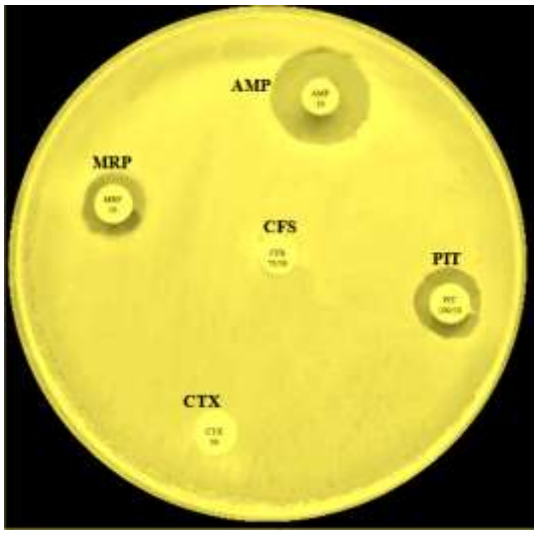


Fig 14: AST by Kirby – Bauer Method (Mueller Hinton Agar) for CoNS

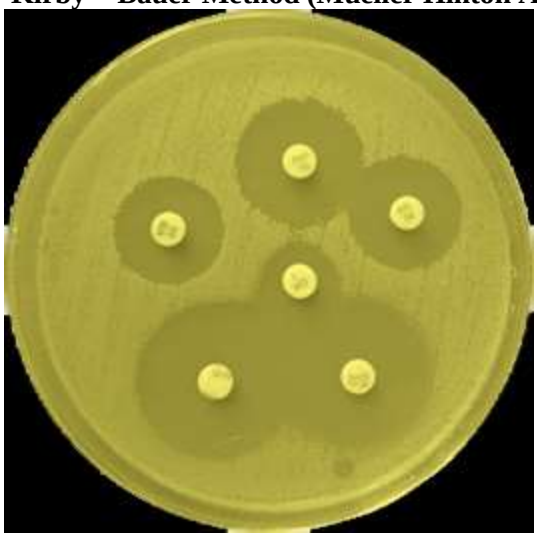


Fig 15: MIC of Vancomycin for S.aureus

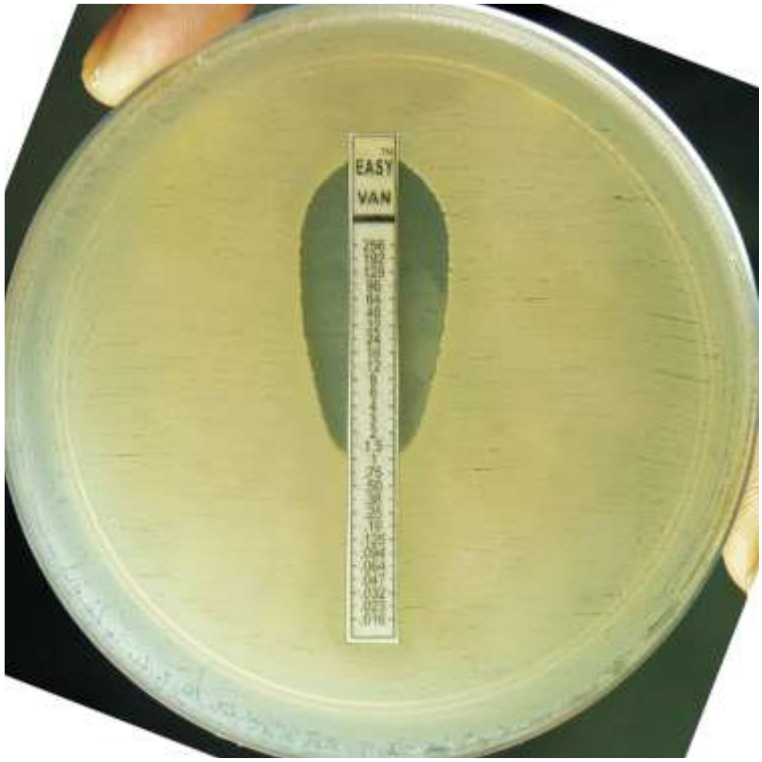


Fig 16: Vancomycin E-Strips shows sensitive pattern for both;
A. Staph aureus (≤ 2µg/ml) B. CoNS (≤ 4 µg/ml)

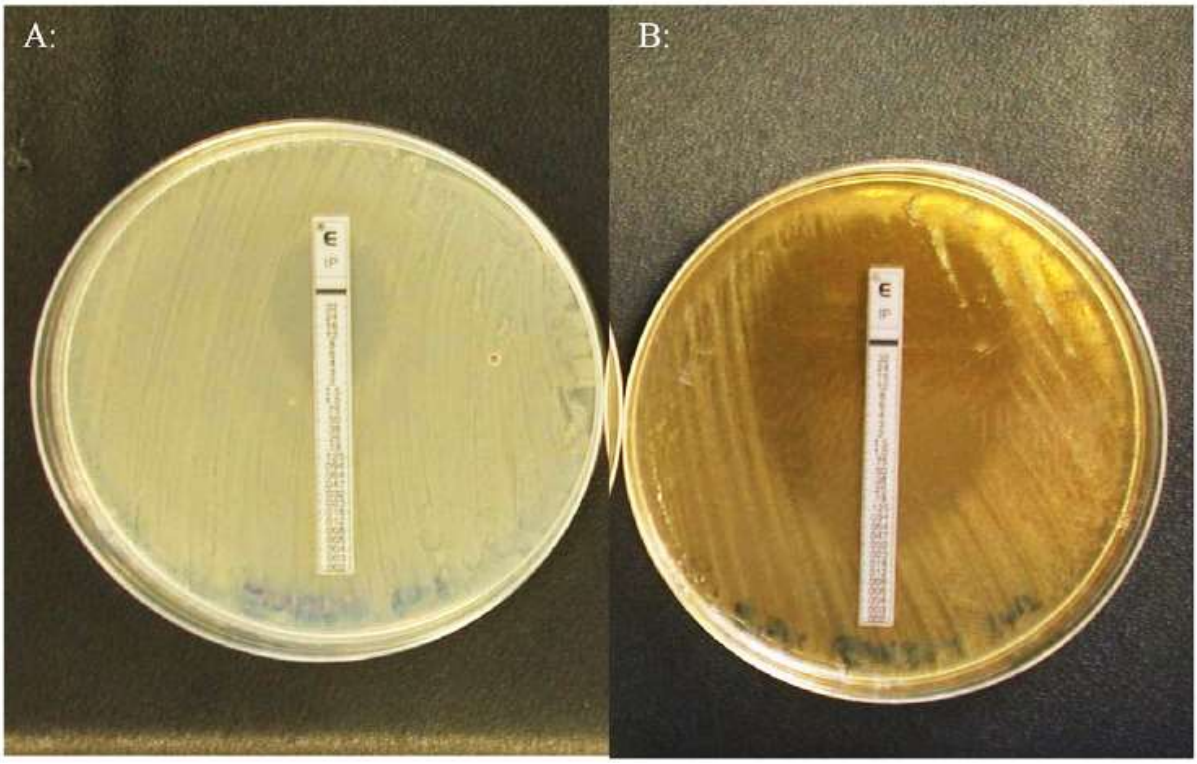


Fig 17: ESBL detection by Combined Disc Method.

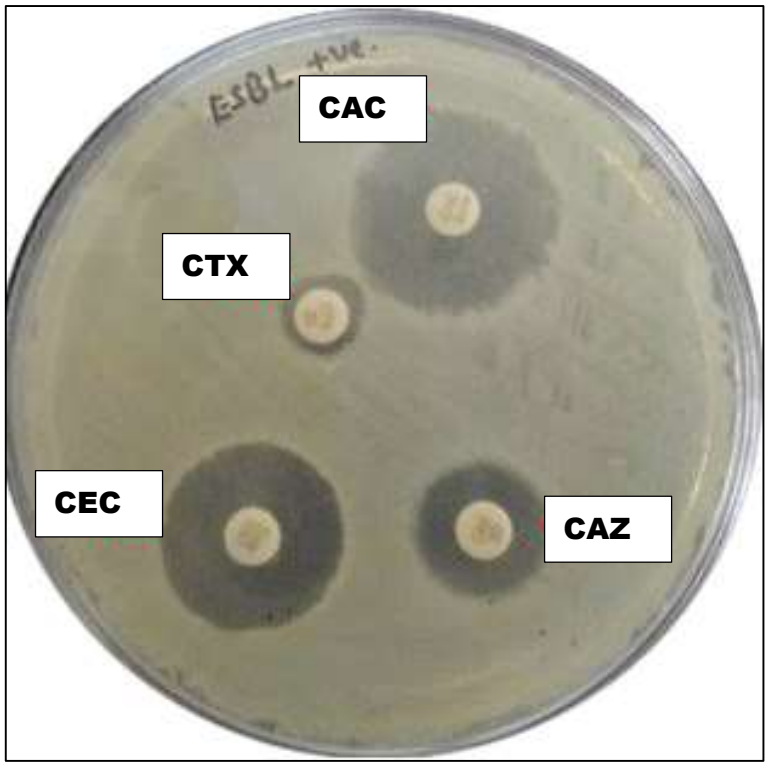


Fig 18: ESBL Detection by E-Strip Method

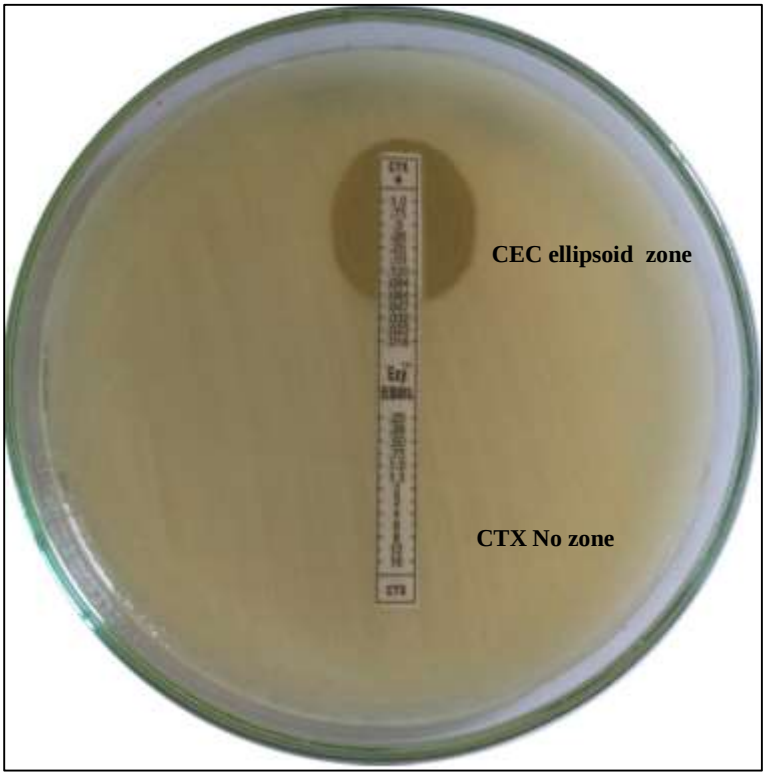
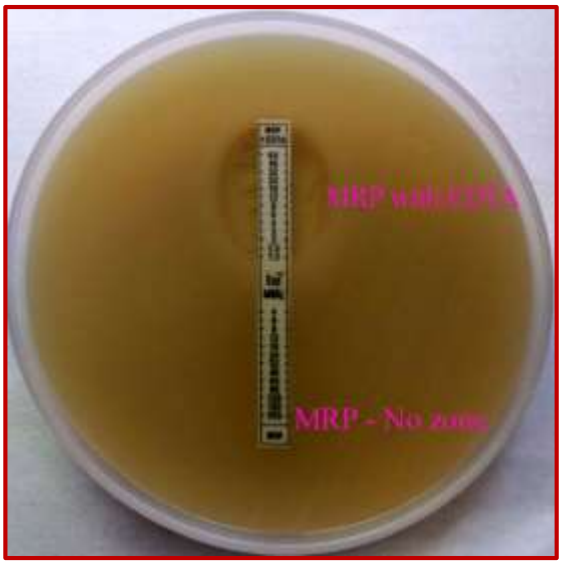


Fig 19: Acinetobacter sensitive to NET-15mm, LE-17mm & TGC-21mm

Fig 20: Detection of MBL resistance pattern in Acinetobacter .

1. Imipenam and Imipenam + EDTA

Fig 21: E-strip method Meropenem with and without EDTA



RESULTS

RESULTS

The study "Ventriculoperitoneal shunt infection in paediatric patients" included a total of 60 paediatric patients who have undergone Ventriculoperitoneal shunt surgery at Coimbatore Medical College for a period of 15 months from March 2017 to June 2018. CSF sample , shunt tip sample and peripheral blood from these patients were cultured and the organisms isolated were identified and analysed for antibiotic resistance pattern.

TABLE 1: DISTRIBUTION OF CASES WITH VP SHUNT INFECTION. (N= 60)

	No of Cases N=60	**Percentage**
CULTURE POSITIVE	10	16.66%
CULTURE NEGATIVE	50	83.34%

Out of 60 patients who underwent Ventriculoperitoneal shunt surgery 10 cases(17%) were culture positive and 50 cases(83%) were culture negative.

Gender distribution was not of much significance except for a slight male preponderance.

TABLE 2 : AGE DISTRIBUTION (n=60)

Age Category	**No of patients**	**Percentage**

Less than 1 year	29	48.3
1 year to 5 years	22	36.7
More than 5 years	9	15.0
Total	**60**	**100.0**

Patients in the age group less than one year had increased risk of infection (48%) when compared with age groups (1 to 5 years) and more than 5 years.

TABLE 3 : CLINICAL PRESENTATION OF PATIENTS WITH VENTRICULOPERITONEAL SHUNT INFECTION

SYMPTOMS	NO OF CASES (N = 60)	PERCENTAGE
FEVER	20	38%
VOMITING	10	17%
INCREASE IN HEAD CIRCUMFERENCE	9	15%
ALTERED SENSORIUM	5	10%
SEIZURES	5	10%
VISUAL DISTURBANCES	4	5%
SHUNT TRACT INFLAMATION	3	5%

Fever is present in 38% of cases , followed by vomiting(17%) and increase in head circumference(15%).

TABLE 4- COMPARISON OF DURATION OF INFECTION AND RISK OF INFECTION (n=60)

DURATION OF INFECTION	NUMBER OF CASES (N = 60)	RISK OF INFECTION
SSI- MEN SURGICAL SITE INFECTION (MENINGITIS &ENCEPHALITIS) (within 90 days of shunt insertion	55	92%
CNS -MEN CENTRAL NERVOUS SYSTEM - (MENINGITIS & ENCEPHALITIS) (after 90 days of shunt insertion)	5	8%

SSI-MEN which includes surgical site infection with signs of both meningitis and encephalitis within ninety days of shunt surgery has highest infection rate (92%) rather than CNS - MEN case.

TABLE 5: INDICATIONS FOR VENTRICULOPERITONEAL SHUNT SURGERY (n=60)

Indications for VP shunt surgery	No of Cases	Percentage
Obstructive hydrocephalus(n=18)	18	30.0
Myelomeningocele with multiple revision (MMC-MR)(n=14)	14	23.3
Preterm with intraventricular hemorrhage(Preterm with IVH)(n=10)	10	16.7
Hydrocephalus following space occupying lesion (H-SOL)(n=5)	5	8.3
Post tuberculosis meningitis (Post – TBM)(n=5)	5	8.3
Post traumatic hydrocephalus (Post Traumatic H)(n=3)	3	5.0
Sporadic hydrocephalus (SH)(n=5)	5	8.3
Total	**60**	**100.0**

Association between the indicators of ventriculoperitoneal shunt surgery and outcome of patient has been analysed and statistically significant P value obtained. Better outcome of survival noted in obstructive hydrocephalus patients with ‘P’ value 0.016. Preterm with intraventricularhemorrhage (Preterm with IVH) is associated with a significant ‘P’ value <0.016.

TABLE 6: REVISIONS ASSOCIATED WITH DIFFERENT INDICATIONS OF VENTRICULOPERITONEAL SHUNT SURGERY (n=10)

EARLY INFECTION (80%)		LATE INFECTION (20%)	
INDICATIONS	**No of cases**	**INDICATIONS**	**No of cases**
POST TUBERCULOUS MENINGITIS	3	OBSTRUCTIVE HYDROCEPHALUS FOLLOWING SOL	1
MYELOMENINGOCOELE	2	SPORADIC HYDROCEPHALUS FOLLOWING SOL	1
PRETERM BIRTH WITH INTRA VENTRICULAR HEMORRHAGE	1		
OBSTRUCTIVE HYDROCEPHALUS	1		
HYDROCEPHALUS FOLLOWING SPACE OCCUPYING LESIONS	1		

Revision surgery is increased in post tuberculous meningitis (37.5%) when compared to hydrocephalus following birth defects, and posterior cerebellar tumours. Among hydrocephalus following birth defects, myelomenigocele is associated with multiple revisions.

TABLE 7: PATHOGENS ISOLATED IN VP SHUNT INFECTION (n=10)

	Isolate	Frequency	Percentage
Gram Positive Organism	CoNS 1 Methicillin sensitive (5) 2 Methicillin resistance (0)	5	50
	Staph aureus MRSA (1) Methicillin resistance	1	10
Gram Negative Organism	E.coli	2	20
	Acinetobacter	1	10
	Pseudomonas	1	10
	Total	**10**	**100**

From total 10 isolates 6 isolates were Gram positive organism and 4 isolates were Gram negative organism.

TABLE 8: DISTRIBUTION OF GRAM POSITIVE COCCI IN VP SHUNT INFECTION

Gram Positive Cocci	No of Cases	Percentage
S.epidermidis	3	50%
S.hemolyticus	1	16.66%
S.lugdunensis	1	16.66%
S.aureus	1	16.68%

CoNS has higher percentage of infection around 83.32% when compared to Staph aureus around 16.68%.

TABLE 9: ANTIBIOTIC SUSCEPTIBILITY PATTERN OF GRAM POSITIVE COCCI

Organism	Penicillin Units	Cefoxitin	Teicoplanin	Gentamicin	Cotrimoxazole	Linezolid	Ampicillin
CoNS n=5	5 (100%)	5 (100%)	5 (100%)	R	4 (80%)	4 (80%)	5 (100%)
Staph aureus n=1	R	R	1 (100%)	R	R	1 (100%)	1 (100%)

All the 5 isolates of CoNS were sensitive to Pencillin, Cefoxitin, Teicoplanin and Ampicillin. 4 isolates were sensitive to Cotrimoxazole. All the 5 isolates of CoNS were resistant to Gentamycin.

Single isolate of Staph aureus was 100% sensitive to Teicoplanin, and Linezolid, wheras it was resistant to Pencillin, Cefoxitin, Gentamicin and Cotrimoxazole.

TABLE 10: ANTIBIOTIC SUSCEPTIBILITY PATTERN OF GRAM NEGATIVE BACILLI

Organism	Ampicillin	Cefoxitin	Ceftazidime	Cefotaxime	Cefoperazone sulbactan	Netilimycin	Gentamicin	Levofloxacin	Tigecycline	Meropenem	Aztreonam	Piperacillin&tazobactam
E.coli	R	100%	R	R	100%	R	R	100%	100%	100%	100%	100%
Pseudomonas	R	R	100%	R	100%	100%	R	100%	100%	100%	100%	100%
Acinetobacter	R	R	R	R	R	100%	R	100%	100%	R	R	R

Two isolates of E.coli was ESBL producers with resistance to Ampicillin, Ceftazidime, Cefotaxime, Netilimycin and Gentamicin. It was sensitive to Cefoxitin, Cefoperazone sulbactan, Levofloxacin, Tigecycline, Meropenem, Aztreonam and Piperacillin & tazobactam.

Single isolate of Pseudomonas was sensitive to all the other drugs except Ampicillin, Cefoxitin, Cefotaxime, and Gentamicin to which it was resistant.

Single isolate of Acinetobacter was sensitive to Netilimycin, Levofloxacin, and Tigecycline. It was resistant to all cephalosporins, carbapenems and monobactam.

TABLE 11: DETECTION OF MINIMUM INHIBITORY CONCENTRATION BY E-STRIP FOR STAPHYLOCOCCUS

S.No	DRUGS	MIC µg/ml		
		Observation	Inference	percentage
1	Vancomycin for Staph aureus (1)	≤ 2	sensitive	17%
2	Vancomycin for CoNS (5)	≤ 4	sensitive	83 %

All the isolates were sensitive to Vancomycin.

TABLE 12 DETECTION OF MINIMUM INHIBITORY CONCENTRATION BY E-STRIP FOR ACINETOBACTER

S.No	DRUGS	CONCENTRATION OF DRUGS	S / R
1	Meropenem	0.0002-32µg/ml	R
2	Colistin	0.016-32 µg/ml	S 0.094 µg/ml

TABLE 13: DETECTION OF ESBL PRODUCTION AMONG GRAM NEGATIVE BACILLI BY VARIOUS METHODS.

S.No	TEST METHOD (n=2)	ESBL DETECTION
1	Screening Method (Standard Disc diffusion) Positive (2)	100%
2	Confirmatory Test (Standard Disc Diffusion) Positive (2)	50%
3	E-Strip Method (2)	100%

Two isolates of E.coli were Extended Spectrum Beta Lactamase producers which was identified by screening method and confirmed by standard disc diffusion method and E-strip method.

Single isolate of acinetobacter was screened with Cefoxitin disc for Metalo Beta Lactamase production and confirmed with disc diffusion and E-strip method but molecular identification is confirmatory.

TABLE 14: ASSOCIATION OF OUTCOME WITH RISK FACTORS

Association of Outcome with Indication of VP shunt	**Outcome**	
	Survival Rate	**Mortality-Rate**
Obstructive hydrocephalus (Obstructive) (18)	18	0
Myelomeningocele with multiple revision (MMC-MR)(14)	12	2
Preterm with intraventricularhemorrhage(Preterm with IVH) (10)	4	6
Hydrocephalus following space occupying lesion (H-SOL) (5)	4	1
Post tuberculosis meningitis (Post – TBM)(5)	5	0
Post traumatic hydrocephalus (3) (Post Traumatic H)	2	1
Sporadic (5)hydrocephalus (SH)	4	1
Total	**49**	**11**

Survival rate after VP shunt surgery is increased in Obstructive hydrocephalus and Mortality rate is increased Preterm with intraventricular hemorrhage.

TABLE 15: OUTCOME OF PATIENTS WITH THE ISOLATED PATHOGEN IN VENTRICULOPERITONEAL SHUNT INFECTION

S.No	Organism	Survival	Mortality Rate	Survival %	Mortality %
1	Gram Positive Cocci (6)	4	2	66.66	33.34
2	Gram Negative Bacilli (4)	1	3	25	75

Survival rate is increased in infection with Gram positive organism and it is drastically decreased in case of Gram negative organism like Acinetobacter, Pseudomonas and E.coli.

CHART 1: DISTRIBUTION OF CASES WITH VP SHUNT INFECTION.

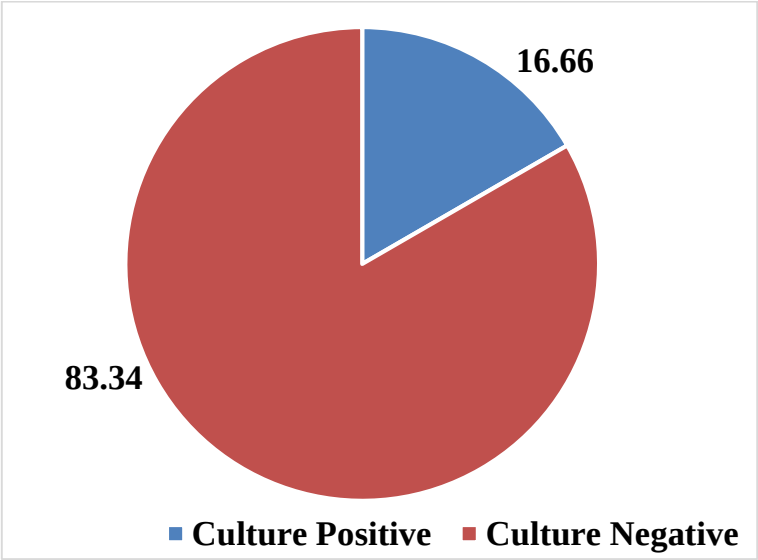


CHART2: AGE DISTRIBUTION

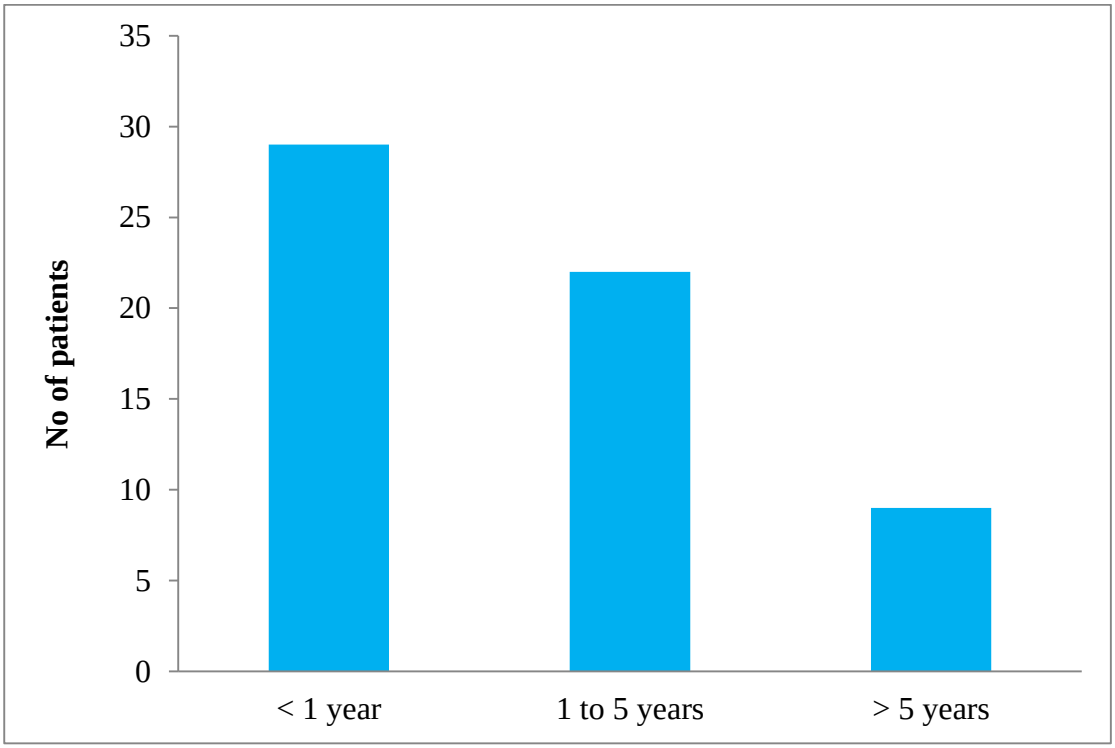


CHART -3 : CLINICAL FEATURES SUGGESTIVE OF VENTRICULOPERITONEAL SHUNT INFECTION

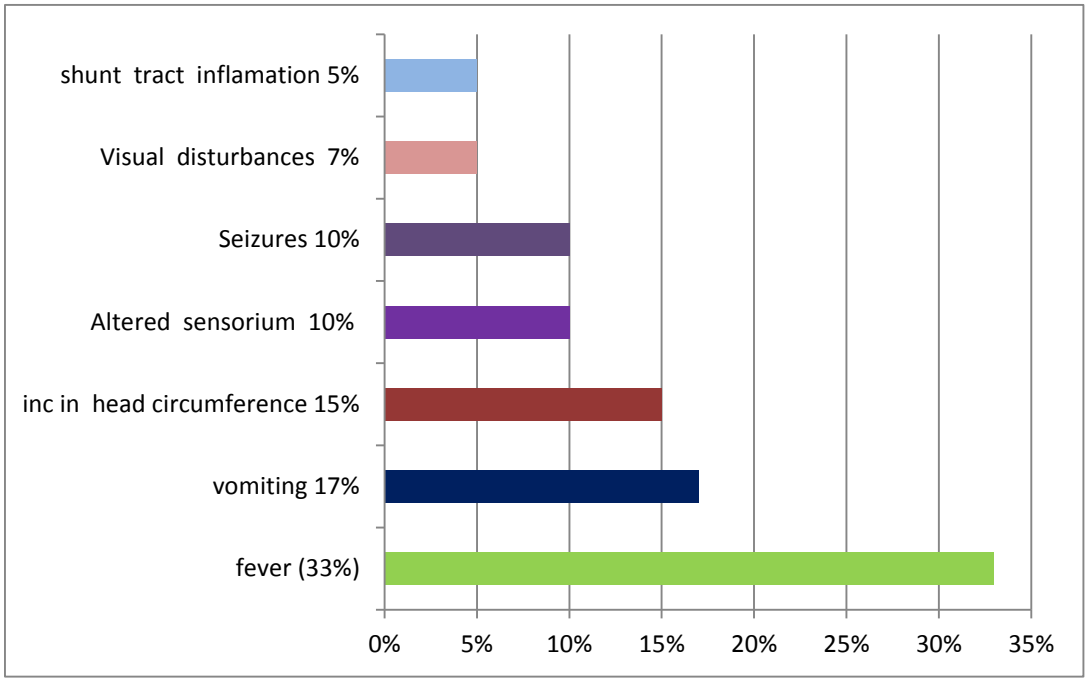


CHART 4: DURATION OF INFECTION

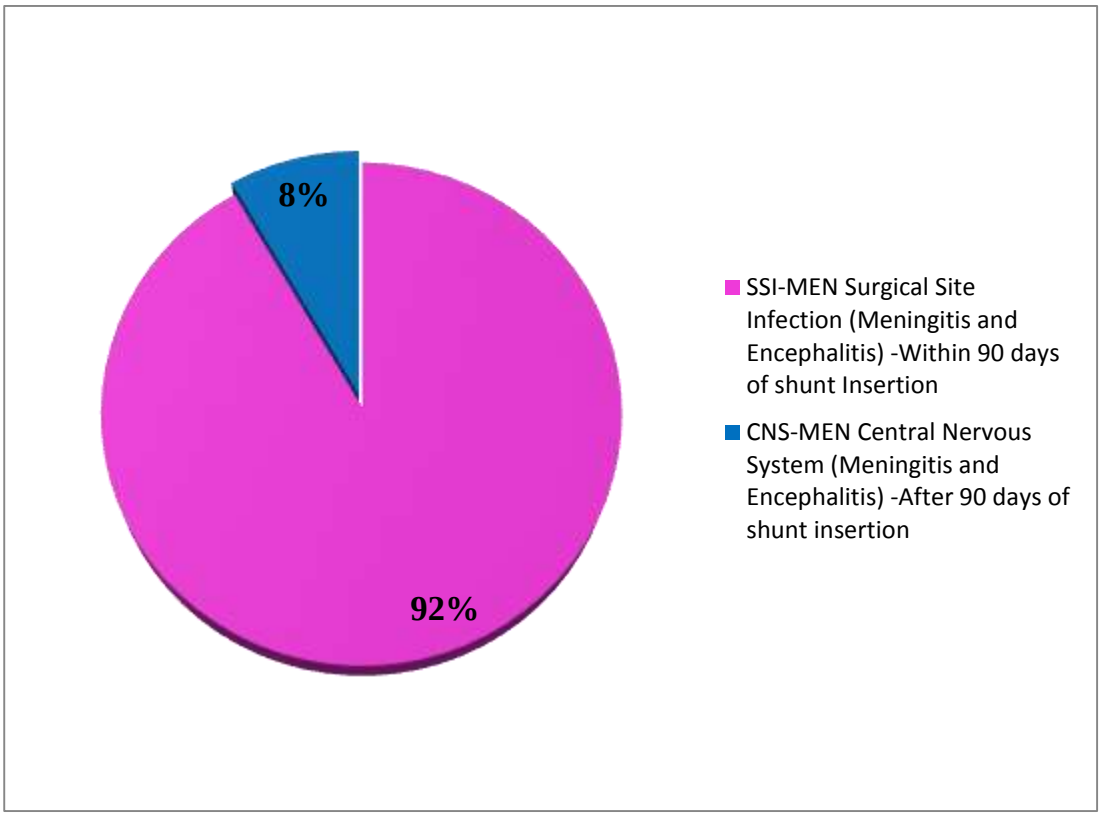


CHART 5: INDICATIONS OF VP SHUNT INFECTION

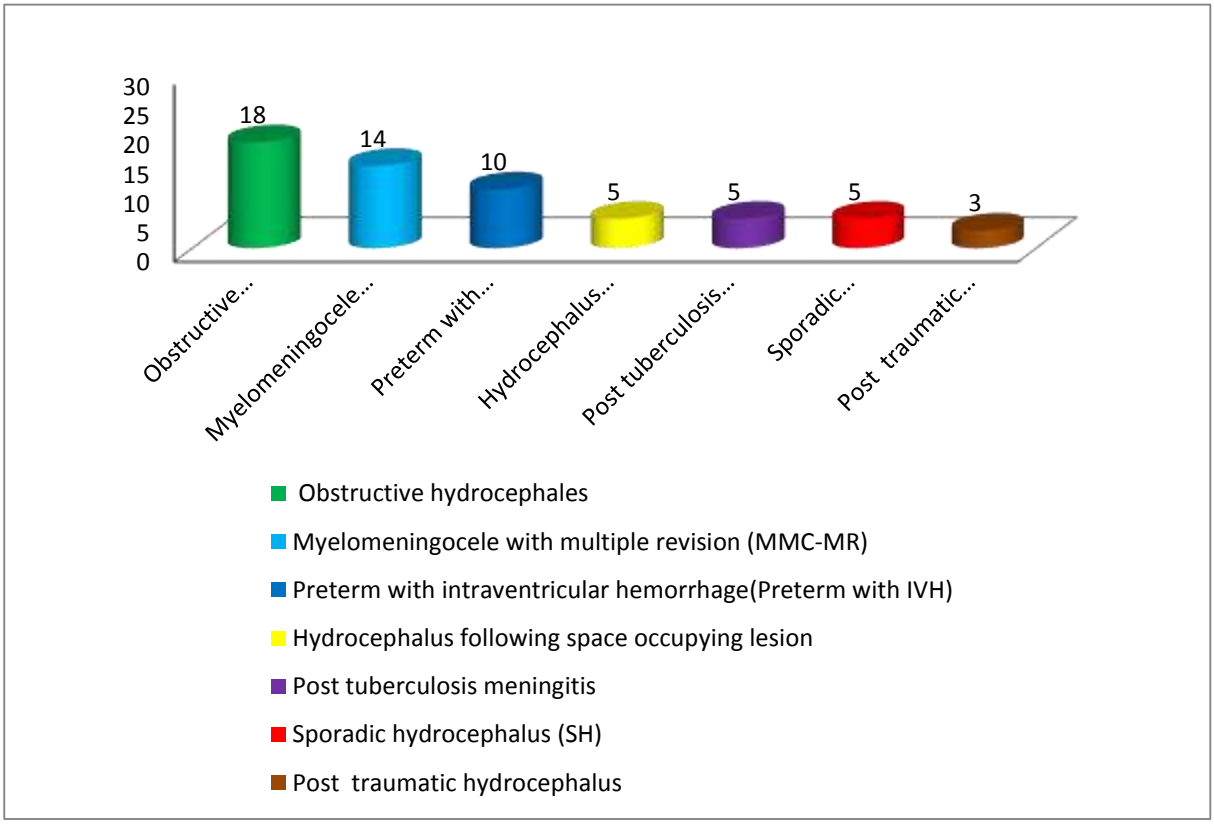


CHART 6 : PERCENTAGE OF REVISIONS IN EARLY AND LATE INFECTION (n=10)

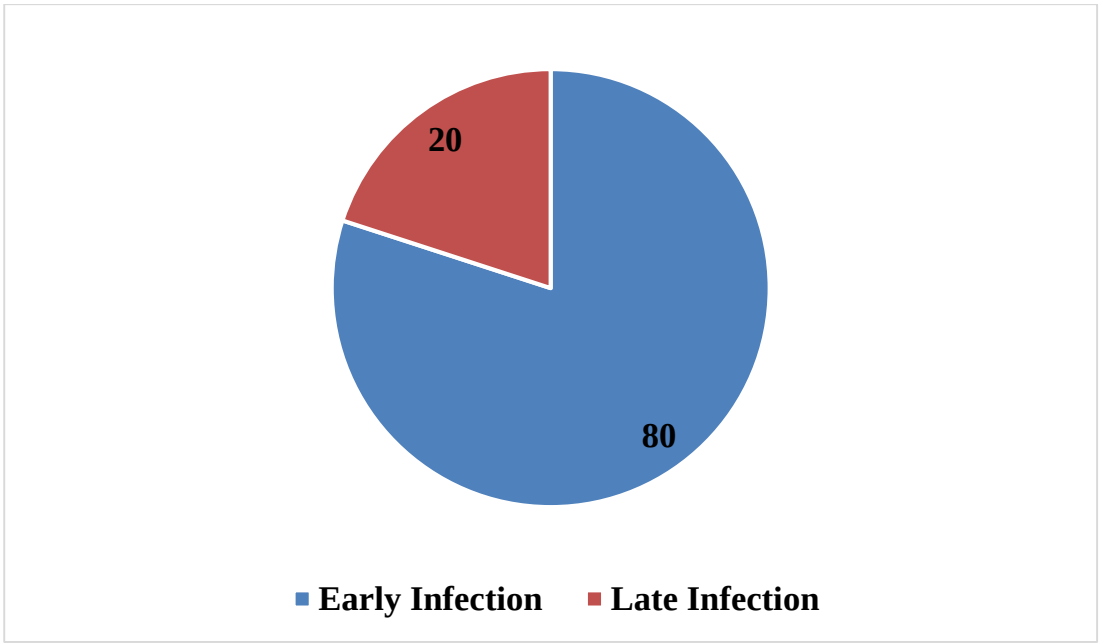


CHART 7: PATHOGENS ISOLATED IN VP SHUNT INFECTION (n=10)

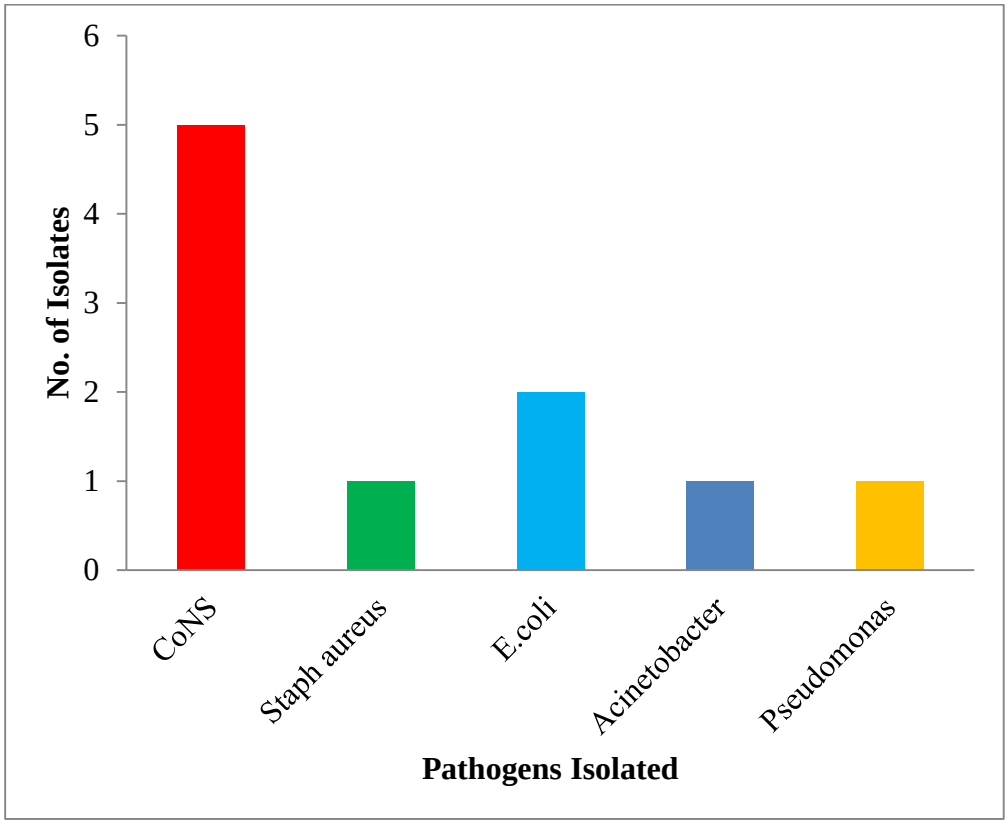


CHART 8 : DISTRIBUTION OF GRAM POSITIVE COCCI IN VP SHUNT INFECTION (n=6)

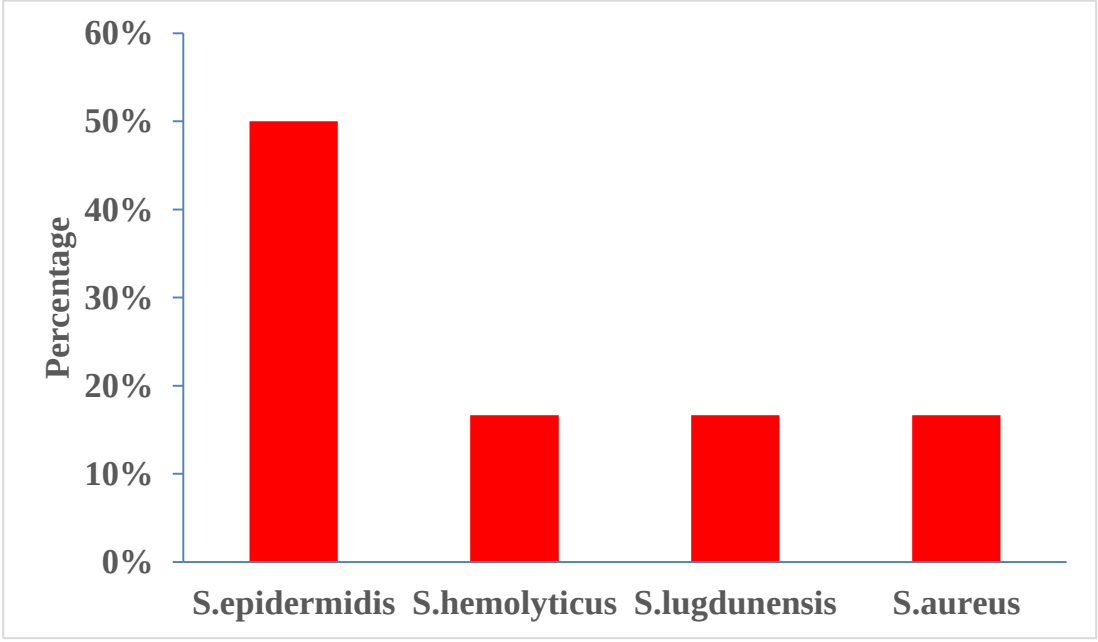


CHART 9: ANTIBIOTIC SUSCEPTIBILITY PATTERN OF GRAM POSITIVE COCCI

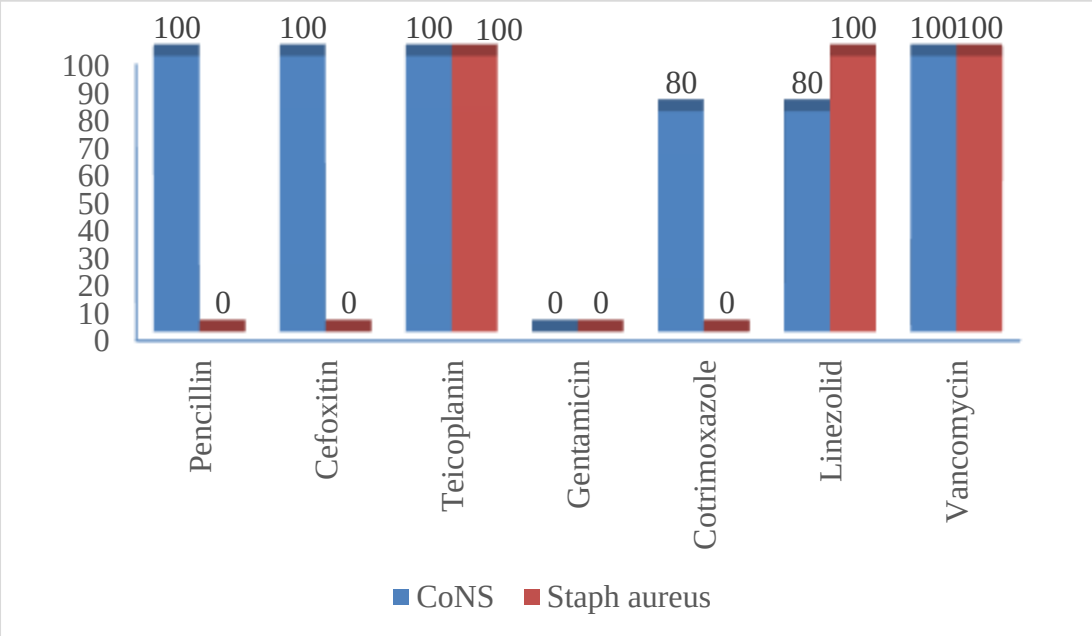


CHART 10: ANTIBIOTIC SUSCEPTIBILITY PATTERN OF GRAM NEGATIVE BACILLI

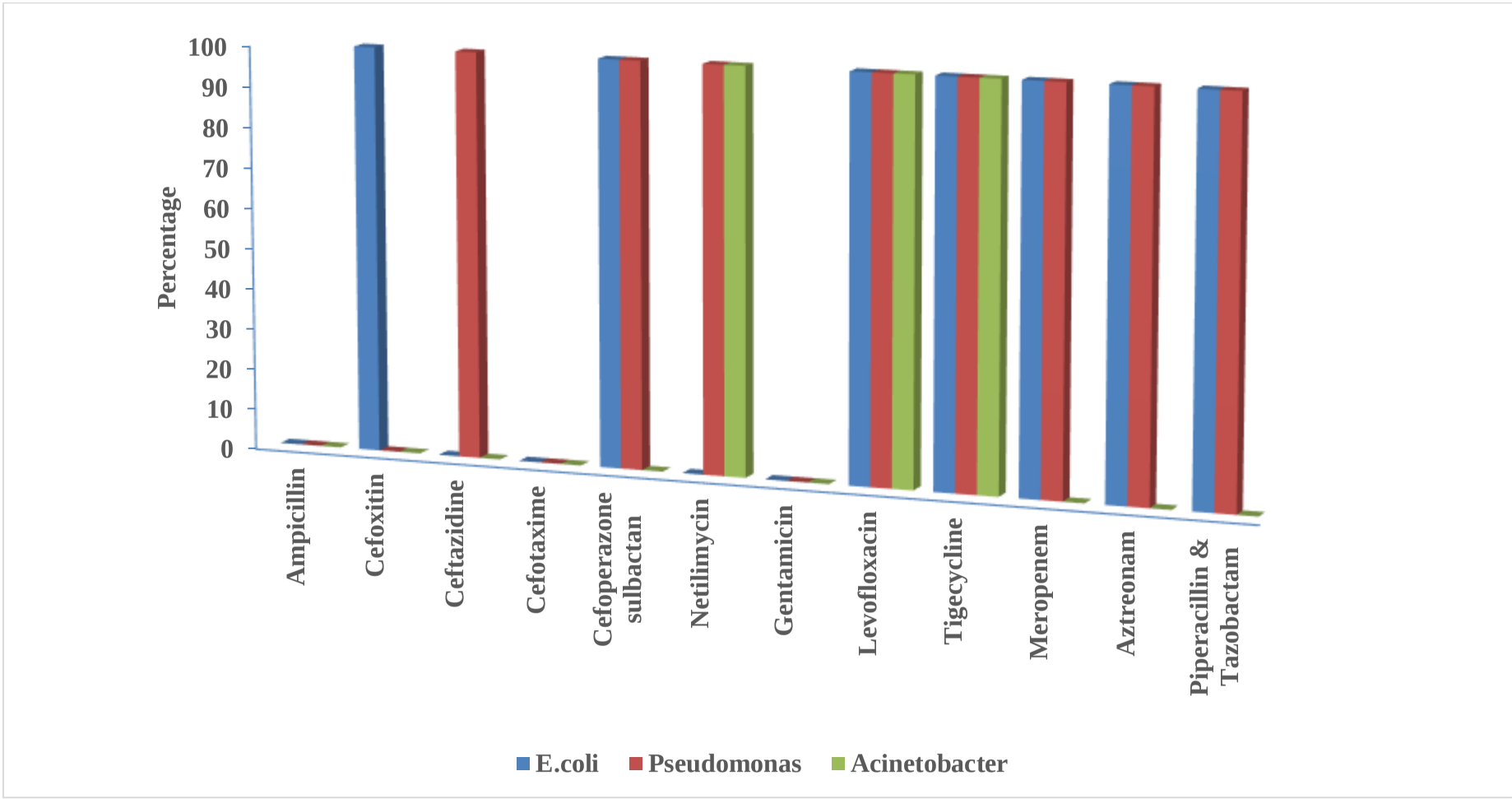


CHART 11- DETECTION OF ESBL BY DIFFERENT METHODS

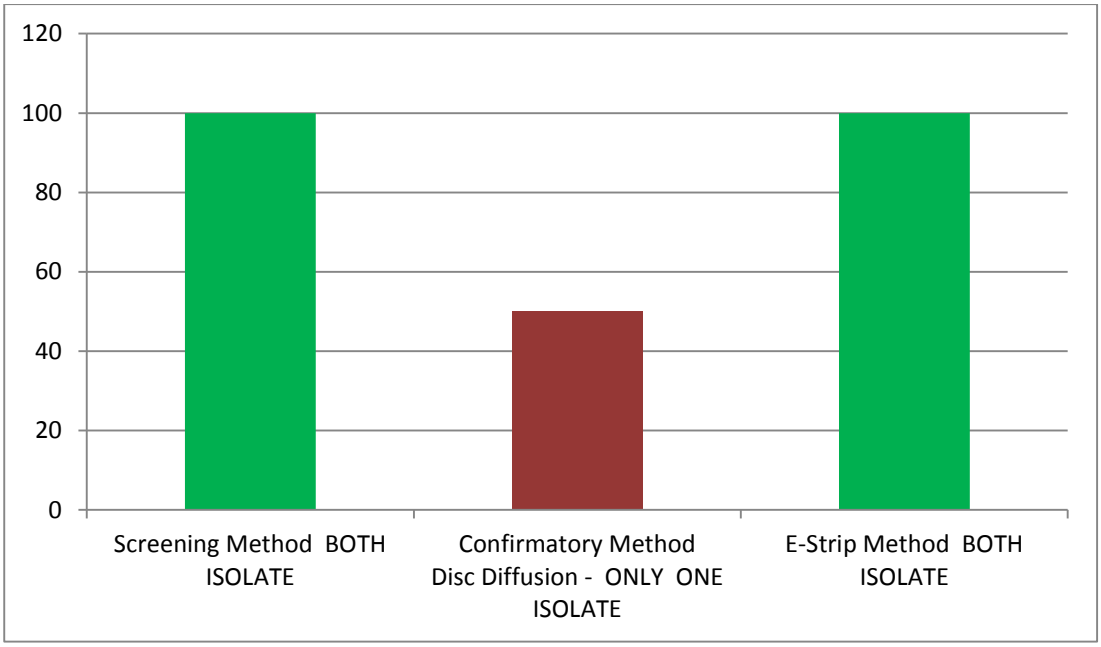


CHART 12: RESISTANCE PATTERN AMONG GRAM NEGATIVE BACILII

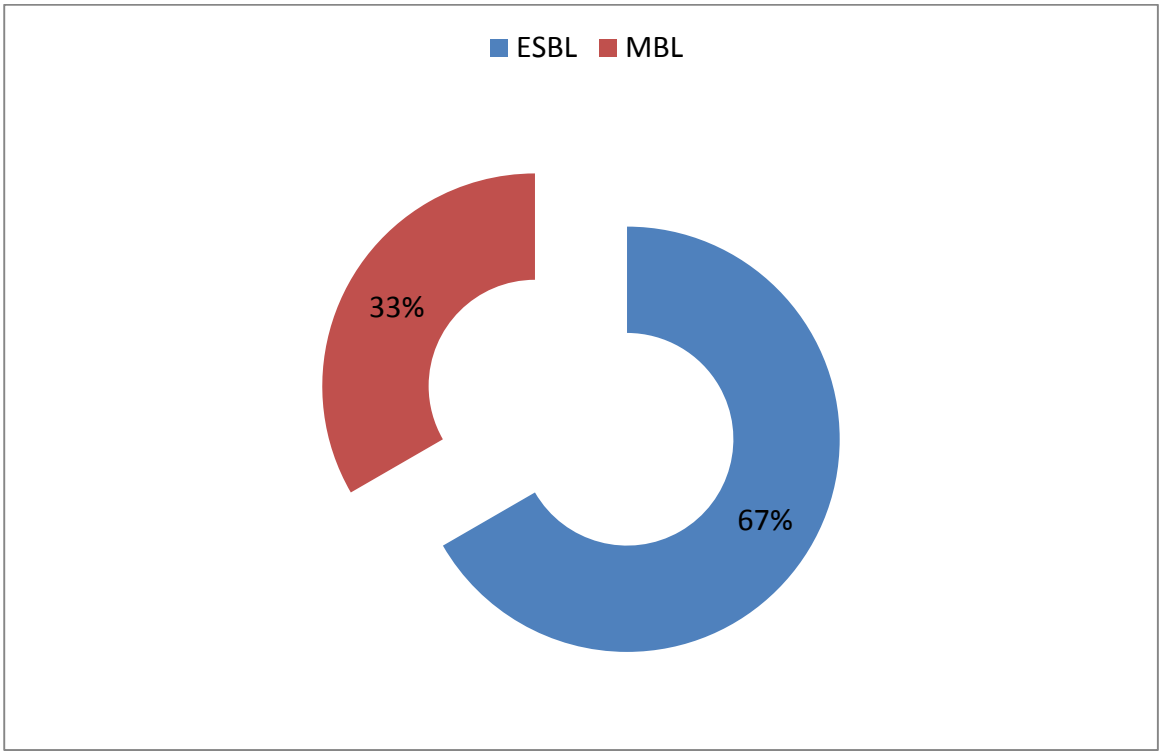
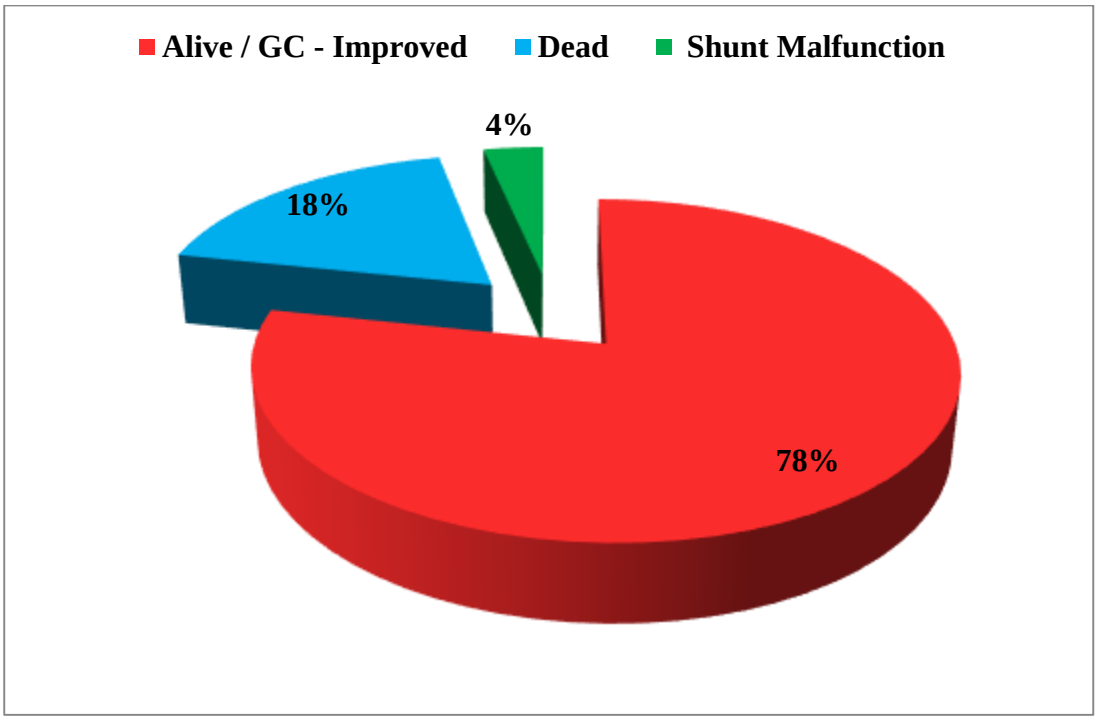


CHART 13: FOLLOW UP FOR 6 MONTHS



DISCUSSION

DISCUSSION

Ventriculoperitoneal shunt surgery is the most common treatment modality for the diagnostic indications of hydrocephalus. This surgery enables drainage of excess cerebrospinal fluid from lateral ventricles into the peritoneal cavity. Shunt infections is one of the predictors associated with significant morbidity and mortality.

This study was done to analyse risk factors, microbial profile of Ventriculoperitoneal infection, the antibiotic sensitivity of the pathogens isolated and clinical outcome of Ventriculoperitoneal shunt infections in paediatric patients.

This study includes clinical samples from 60 paediatric patients following Ventriculoperitoneal shunt surgery. 10 (16.66%) of the cases were culture positive and 50 (83.34%) cases were culture negative. The incidence rate in this study is 16.6%. The incidence of infection was in concordance with the study of Anna Conen et al, where incidence rate is (1 % to 18%). and study by Xing Wu et al[76], where incidence rate is from (2 % to 39%). A study by Dharmajaya et al[21] showed the rate of infection to be 5% in Haji Adam Malik Hospital (Reference centre for VP shunt surgery, North Sumalda) in contrast. This hospital documented the fact that low-levels of preoperative albumin was a significant factor in increasing the infection. Use of antibiotic impregnated shunts in referral centre leads to decline in infection rate.

In this study, male population constituted 57% and females constituted 43%. Gender distribution was not of much significance except for a slight male preponderance. This is supported by a study conducted by Vikas Kumar et al[71] at G.B .Pant Post Graduate Institute where 64% of Ventriculoperitoneal shunt surgery was done in males. This gender dimorphism is due to hormonal changes and inbuilt susceptibility to infections in male population. A study done by Tamara D and Simon et al[66], is in contrast "where infection rates following CSF shunt placement across paediatric hospitals in the United States", showed an increased risk of infection in female sex.

In this study 60 paediatric patients are included, of which 29 cases (48%) were reported to have primary shunt insertion at less than one year of age. 22 patients (37%) had Ventriculoperitoneal shunt insertion at age between 1 to 5 years and 9 patient (15%) were above 5 years. In a study conducted by Matthew J et al, the independent risk factors for shunt infection was studied and significant P value was obtained. His study suggested that each decreasing year of patient age was associated with 4% increase in the risk of shunt infection and insertion of a Ventriculoperitoneal shunt in a premature infant was associated with five fold increase in the risk of infection. This finding is consistent with our study where majority of patients were < 1 year. Incidence is high in premature infants because of following reasons:

1) Immature immune system

2) Poor skin barrier

3) Altered skin bacterial density

4) Co –morbidity

CDC (2018) guidelines defines shunt infection as; 1) SSI-MEN (Surgical site infection which includes both meningitis and encephalitis) within ninety days of infection and 2) CNS -MEN (Central Nervous System which includes both meningitis and encephalitis) after ninety days of infection. In this study 55 cases (92%) of cases where reported as SSI-MEN and 5 cases (8%) were reported as CNS- MEN. In a study conducted by Wellingson Silva et al[74], 90% of VPS infections were identified at first three months, this reinforces the fact that these infections are a result of skin commensals at the surgical site in Gram Positive Cocci infections and retrograde infections from bowel in case of Gram Negative infections.

In this study, clinical features of patients were analysed. Fever (38%), vomiting (17%), increase in head circumference in 15%, altered sensorium (8%), seizures (8%), visual disturbance (6%) and shunt tract inflammation was noted in 5%. In a study conducted by Mwang Ombe et al similar clinical features were noted of which fever, irritability and vomiting were the most common features. Abdominal distension was also noted in few of the paediatric patients.

The etiology of hydrocephalus in paediatric age group who required shunt surgery were; 1) congenital malformations (Myelomeningocele 23% and Obstructive Hydrocephalus 30%), 2) Gestational defects 17% (Preterm with Intra Ventricular Hemorrhage), 3) hydrocephalus following tuberculous meningitis 8.3%, 4) trauma (5%), 5) posterior cerebellar fossa tumours (8.3%) and 6) sporadic causes(8.3%).

In a study conducted by Tamara D Simon et al[66], the following indications for CSF shunt placement was documented, Myelomeningocele (21%), IVH (15%), Aqueductal stenosis (12%). The percentage in Obstructive causes and IVH are increased in this study, which indicates that Anti –natal screening program must be improved with intake of folic acid to prevent neurological complications.

In this study, statistically significant P value has been obtained for two independent risk factors. For Obstructive hydrocephalus 0.016 and 0.001 for Preterm with IVH. In a study conducted by Matthew J. McGirt[46], the P value for premature birth is 0.0002 which is similar to this study. This could be attributed to poorly developed immune system and the high density of bacteria on premature skin.

In this study following VP shunt surgery ,symptomatic cases of infection were 60 .Out of which 48 cases had primary Ventriculoperitoneal shunt surgery and 12 cases underwent Revisions. . Revision shunt surgeries were increased in hydrocephalus following tuberculosis meningitis (38%) and Myelomeningocele (25%). A study

conducted by Vikas Kumar in Neurosurgical unit for a period of six years included 1186 VP shunt surgeries[71]. 259 (21.8%) cases underwent shunt revisions with 83 cases (24%) of tuberculous meningitis as a leading etiology for revision surgery. Poor general conditions of the patient and high cellular content of CSF are the important reasons for revisions in tuberculous Ventriculoperitoneal surgery .

Incidence of Ventriculoperitoneal shunt infection varies from (3 - 13 %), in the Western world and in United Kingdom 5.2% infection rate was documented. In this study, the incidence rate was 17 % with 60 % of infection caused by Gram Positive Cocci and 40 % of infections caused by Gram Negative Bacilli .After speciation of Gram Positive Cocci, it was found that CoNS showed a higher percentage of infection around 83.32% when compared to Staph aureus (16.68%).In a study done by Sarguna et al[61], Shunt associated infections(65%) are caused by Coagulase Negative Staphylococcus (CoNS) and 19 to 22% of infections were caused by Gram Negative Bacilli.

CoNS (65%) was the most common organism causing VP shunt infection . This study is in concordance with Sarguna et al study[61]. Among 5 isolates of CoNS, 3 isolates were S.epidermidis and 1 isolate of S.hemolyticus which hydrolysed urea was documented. Single isolate of S.lugdunensis which produces clumping factor is negative for tube coagulase and DNase test. S.lugdunensis is an emerging pathogen in VP shunt infections. In a study by J.A.T Sandoe and Longshow, 50% of VP

shunt infections were caused by CoNS, due to its affinity to adhere to plastics. The above study suggest that CoNS are low virulence pathogens but S.lugdunensis are aggressive organisms with tendency to cause opportunistic infection. CoNS infections are indolent and subacute in presentation, with a tendency to form biofilm. Treatment involves removal of shunt with administration of intrathechal antibiotics.

CoNS infections are associated with biofilm formation when plastic indwelling devices are placed in sterile sites. The characteristic feature of biofilm formation is initiated by adherence and proliferation of the organism due to virulence factor coded by PSM genes. Phenol Soluble Modulins leads to maturation of the biofilm, detachment and sepsis.

All the 5 isolates of CoNS were sensitive to Pencillin, Cefoxitin, Teicoplanin and Vancomycin. 4 isolates were sensitive to Cotrimoxazole and 3 isolates were sensitive to Ciprofloxacin. All the 5 isolates of CoNS were resistant to Gentamicin .

One isolate of Staph aureus was 100% sensitive to Teicoplanin, Linezolid, Vancomycin whereas it was resistant to Pencillin, Cefoxitin, Gentamycin, Ciprofloxacin and Cotrimoxazole. Minimum Inhibitory Concentration (MIC) of Vancomycin by E-strip for Staph aureus and CoNS was done and all the 6 isolates were 100% sensitive to Vancomycin.

All the two isolates of E.coli were ESBL producers with resistance to Ampicillin, Ceftazidime, Cefotaxime, Netilimycin and Gentamicin. It

was sensitive to Cefoxitin, Cefoperazone sulbactan, Levofloxacin, Tigecycline, Meropenem, Aztreonam and Piperacillin & tazobactam.

The single isolate of Pseudomonas was sensitive to Ceftazidime, Cefoperazone sulbactan, Netilimycin, Levofloxacin, Tigecycline, Meropenum, Aztreonam and Piperacillin & tazobactam. It was resistant to Ampicillin, Cefoxitin, Cefotaxime, and Gentamicin. Blood culture was also positive for Pseudomonas in this patient and the patient died of septicaemia.

Acinetobacter baumanii ,single isolate was sensitive to Netilimycin, Levofloxacin, and Tigecycline . It was resistant to all cephalosporins, carbapenems and Monobactam. The patient is a 5 year old boy who underwent repeated revisions following meningioma of sphenoid wing. The acinetobacter isolated was a Metallo Beta Lactamase producer, which was screened and confirmed by Disk diffusion (Imipenem and Imipenem with EDTA). Further confirmation with E-strip (Meropenem with and without EDTA) was done. However the patient succumbed following third revision.

Survival rate is increased in infection with Gram Positive Cocci 67% and it is drastically decreased in case of Gram Negative Bacilli 25% (E.coli, Acinetobacter, and Pseudomonas).

Follow up of the 60 patients who underwent Ventriculo peritoneal shunt surgery was done of which 47 cases survived with better neurological outcome. 11 patients died and 2 patients had shunt malfunction.

Though the treatment is mostly shunt removal followed by temporary CSF divergence with EVD, the duration of antibiotic therapy and the length of time during which the shunt is exteriorised is of much significance. This is especially so with MDR pathogens and may lead to complications like recurrence, revision, meningitis, ventriculitis and encephalitis leading to increased mortality. Loss of IQ with increased risk of seizures due to neuronal death.

Of late antibiotic impregnated shunts with Rifampicin/Clindamycin are used which kill the bacteria rather than preventing adherence. EVD with silver impregnated drains have also come into vogue and these in turn prevent initial adherence of organisms. Hydrogels which reduce microbial viability without causing cytotoxicity have been advocated recently.

Prevention is by following institutional standardized protocols hand washing, double gloving, decreasing bacterial load of patient's skin, minimal shunt handling and peri-operative antibiotics where Microbiology plays a significant role.

SUMMARY

SUMMARY

- This study was done for a period of 18 months involving 60 paediatric patients of both gender and age group below 13 years.
- VP Shunt surgery was done in 48 patients and about 12 patients had undergone VP shunt revisions.
- 10 patients were infected giving an infection rate of 16.6%.
- The study included 57% males and 43% of females.
- Diagnostic indication for hydrocephalus necessitating shunt surgery were; 1) Congenital malformations (53%), 2) preterm and IVH (17%), 3) Hydrocephalus following tuberculous meningitis (8.3%), 4) trauma (5%), 5) Posterior cerebellar fossa tumours (8.3%), 6) Sporadic cases (8.3%).
- The clinical features of patients with shunt malfunction included fever, vomiting, increase in head circumference, altered sensorium, seizures, visual disturbances and shunt tract inflammation.
- Majority of shunt infections occurred within a period of 90 days of shunt infection (92%) and most of infections occured in age group of less than one year (48%).
- In this age group (<1 year) obstructive hydrocephalus and preterm with IVH were found to be significant risk factors.
- VP shunt surgery improved the survival rate of patients with obstructive hydrocephalus.

- Revision surgery is significantly increased in post tuberculous meningitis (37.5%) when compared to hydrocephalus following birth defects and posterior cerebellar tumours.
- The common pathogen isolated was CoNS (83%), and other pathogens are staphylococcus aureus (16.68%), E.coli (20%), Acinetobacter (10%) and pseudomonas (10%).
- Gram Positive cocci were 100% sensitive to Vancomycin and sensitivity of Vancomycin by E-strips for S.aureus was less than 2 mg/ml and for CoNS it was less than 4mg/ml.
- Both MIC and Disc diffusion methods demonstrated resistance to Meropenem. The MIC for colistin was done and it was sensitive.
- Among Gram Negative Bacteria, ESBL accounted for 50%, and MBL for 25%, pseudomonas was 100% sensitive to ceftazidime and Piperacillin with Tazobactam.
- Emergence of MDR isolates have necessitated molecular diagnostics such as PCR which enhance rapid identification of shunt infected pathogens.
- Treatment protocol followed was shunt removal, intravenous antibiotic therapy and shunt reinsertion was done after seven days in CoNS infection, in case of GNB infection antibiotics was extended upto 14 to 21 days with extraventricular drain.
- Survival rate was increased in Gram Positive Cocci infections (67%) when compared to Gram Negative Bacilli infections.

CONCLUSION

CONCLUSION

- Ventriculoperitoneal shunt infection is one of the major complications associated with mortality and morbidity resulting in neurological disturbances.
- The infection rate in patients with ventriculoperitoneal shunt was 16.66%.
- A large number of infections occurred in children with congenital malformations and preterm with intraventricular hemorrage.
- Most of the infections occurred within three months of surgery.
- Staphylococcus epidermidis was the commonest pathogen isolated and survival rate is more in gram positive infections.
- Promising results are obtained by early removal of the shunt hardware accompanied by appropriate antibiotic therapy until CSF culture turns negative, followed by shunt replacement.
- With the emergence of methicillin resistant strains, ESBL and MBL producers, diligent use of antibiotics will restrict the spread of drug resistant strains in the community and environment. Determining MIC with E-strips are extremely useful in these cases and will go a long way if implemented in routine use.
- Infection Control Committee at the Institutional level plays a significant role in framing antibiotic policy and standardization of protocol to be followed in such infections thus limiting the spread of these drug resistant nosocomial pathogens.

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ANNEXURES

PROFORMA

Name :

Age :

Sex :

Address :

History of Preterm Birth :

History of Repeated Shunt Surgery :

Complaints of Fever :

Complaints of Vomiting :

Complaints of Neck Stiffness :

Complaints of persistent cry :

Complaints of poor feeding :

Signs suggestive of Ascites :

Signs suggestive of Neuromotor Deficit :

STATEMENT OF CONSENT

I, ……., do hereby volunteer and consent to participate in this study being conducted by Dr. M. Sangeetha, I have read and understood the consent form (or) it has been read and explained to me thoroughly. I am fully aware of the study details as well as aware that I may ask questions to her at any time.

Signature / Left Thumb Impression of the Patient
Station: Coimbatore
Date:

Signature / Left Thumb Impression and name of the witness
Station: Coimbatore
Date:

STATEMENT OF CONSENT

I, _____, do hereby volunteer and consent to participate in this study being conducted by Dr.M.Sangeetha , I have read and understood the consent form (or) it has been read and explained to me thoroughly. I am fully aware of the study details as well as aware that I may ask questions to him at any time.

Signature / Left Thumb Impression of the patient

Station: Coimbatore

Date:

Signature / Left Thumb Impressionand Name of the witness

Station: Coimbatore

Date:

ஒப்புதல் படிவம்

பெயர் ..... வயது .....

முகவரி .....

ஆகிய நான் நுண்ணுயிரியல் துறை மருத்துவக் கல்லூரி பட்ட மேற்படிப்பு மாணவி மரு. சங்கீதா. ம அவர்கள் குழந்தைகளுக்கான வென்ட்ரிபெரிடோனியல் புற தொற்று கிரிமிகள் என்ற தலைப்பில் செய்யும் ஆய்வில் என் குழந்தையை ஆய்வு செய்ய சம்மதிக்கிறேன். இந்த ஆய்வில் செய்முறை மற்றும் இது தொடர்பான அனைத்து விளக்கங்களையும் கேட்டுக்கொண்டு எனது சந்தேகங்களையும் தெளிவுபடுத்தி கொண்டேன் என்பதையும் தெரிவித்துக்கொள்கிறேன்.

இந்த ஆய்வில் என் குழந்தையை உட்படுத்த முழு மனதாக சுய சிந்தனையுடன் ஒத்துக்கொள்வதுடன் எந்த நேரத்திலும் இந்த ஆய்வில் இருந்து விலகிட எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இந்த ஆய்வில் என் குழந்தையின்.விவரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக்கொள்கிறேன்.

இடம்:

தேதி:

கையொப்பம் கைரேகை

MASTER CHART

S.No	M.No /Date	Name	Signs of ABM	Indication of VP Shunt	Age of 1st VPS surgery	CSF Sample 1			Sample 2Shunt Tip			Sample 3Blood			Early Infection within 90 days of Shunt surgery	Late Infection after 90 days	Repeated Shunt Infection	Org. visible in		Growth in CSF Sample	Growth in Shunt Tip	Growth in Blood	Biochemical Reactions InVic	Anaerobic Culture	Biochemical Analysis				CSF Cytology <5 (normal)	Isolate	sensitivity	intermediate	resistance	Type of Resistance Pattern Intermediate Resistance	Follow up for 6 months
						I DOS	II RVS	III RVS	I DOS	II RVS	III RVS	I DOS	II RVS	III RVS				Org. visible in	Organ						Glucose 40-70mg/dL	Albumin upto 15 mg/dL	Protein 15-50mg/dL	LDH <-70 mg/dL							Morbidity /Mortality
1	M-78	Praneeth	+	O	4mon Obst Hydro	6mon 06/06/17	-	-	6mon 06/06/17	-	-	6mon 06/06/17	-	-	✓		-	-	Few GNB	NG	NG	NG	NIL	NG	↓	↑	↑	N	↑	NG					Alive GC↑
2	M-79	B/O Deivani	+	P	D35	5TH POD 06/06/17	-	-	5th POD 6/6/17	-	-	5th POD 6/6/17	-	-	✓			Few	-	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
3	M-173	B/O Jayasutha	+	O	21/2 Months	10th POD 09/06/17	-	-	10th POD 9/6/17	-	-	10th POD 9/6/17	-	-	✓			Moderate	-	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
4	M-660	Hariprasad raj	+	O	2Yrs/mon	5TH POD 12/06/17	-	-	5th POD 12.6.17	-	-	5th POD 12.6.17	-	-	✓			Few	Few GNB	LF/GWC	LF/GWC	LF/GWC	SUPPORTING	NG	↓	↑	↑	↑	↑	E.coli	PIT ,MRP	-	IP, COT, LE, AK	ESBL	Alive GC↑
5	M-841	B/O Arumani	+	P	D40	5TH POD 12/06/17	-	-	5th POD 12.6.17	-	-	5th POD 12.6.17	-	-	✓			Few	Few GNB	-	-	-	NIL	NG	↓	↑	↑	↑	N	NG					Alive GC↑
6	M-4737	B/O Kanjana	+	MMC	D 45of birth	5TH POD NG	2 month after 1 vps 24/07/17	-	NG	2 mon after IVPS 24.7.17	-	NG	2 mon after IVPS 24.7.17	-	✓			Moderate	-	-	-	-	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
7	M-4740	Rani	+	PTB M	4yrs	10TH POD 24/07/17	10/18/2017	-	Shunt removed 24.7.17	18.10.17	-	24.7.17	18.10.17	-	✓			Many	-	-	-	-	NIL	NG	↓	↑	↑	↑	Lymphocy	NG					Alive GC↑
8	M-4927	SUBIKSHA	+	MMC	D45	6 month NG	11 month 03/08/17		6 month 03/08/17	11 mnth	-	6 month NG	11 mon 3.8.17	-		L		Few	-	-	-	-	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
9	M-4951	B/O Muthukumar	+	P	D40	5TH POD 04/08/17	-	-	5 POD 4.8.17	-	-	5 POD 4.8.17		-	✓			Few	Few GNB	-	-	-	NIL	NG	↓	↑	↑	↑	↑	NG					Dead on 10th POD
10	M-5001	Dharshana	+	PTB M	2Yrs/mon	10TH POD 07/817	10/10/2017		10TH POD 7.8.17	20/10/17	-	POD 10 7.8.17	10/10/2017	-	✓			-	Few GNB	-	-	-	NIL	NG	↓	↑	↑	↑	Lymphocy	NG					Alive GC↑
11	M-5091	Mala	+	SP H	1ST year of life	3RD YEAR	5Th yr 10/08/17	-	3rd Year	5th years 10.8.17	-	3rd Year	5th Yr 10.8.17	-		L		Few	-	-	-	-	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
12	M-5092	Vaishnavi	+	MMC	d45	11 month 10/08/17		-	11 mon 10.8.17		-	11 mon 10.8.17		-		L		Few	-	-	-	-	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
13	M-5136	Davidraja	+	MMC	d35	31/2 MONTHS 12/8/17	-	-	31/2 mon 12.8.17	-	-	31/2 mon 12.8.17		-	✓			Few	Few GNB	LF/GWC	LF/GWC	LF/GWC	SUPPORTING	NG	↓	↑	↑	↑	↑	E.coli	-		PIT, MRP, CFS,CIP, COT, LE, AK, G	ESBL and AmpC	Dead
14	M-5276	Akilesh	+	O	4 monthof age	10th pod 18/08/17	-	-	10TH POD 18.8.17	-	-	10TH POD 18.8.17		-	✓			Few	Few GNB	-	-	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
15	M-5504	Sadapidipan	+	SOL	5 yrs	after 6months of VPS surgery 29/08/17	-	-	After 6 month 29.8.17	-	-	After 6 month 29.8.17	-	-		L	_	Few	-	-	-	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
16	M-5678	priyanka	+	MMC	D 45	10th POD NG	6 Month NG	DOS 21/2 y 6.9.17	-	NO SHUNT SAMPLE		-	6.9.17		✓	-	_	Few	No	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑
17	M-6658	B/O kuppu	+	MMC	D 45	15th POD 13.10.17	-	-	15th POD 13.10.17	-	-	15th POD 13.10.17	-	-	✓	-	_	Few	NO	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG	-	-			Alive
18	M-6786	B/O Saranya		O	D 45	2 month 19.10	-	-	2 month 19.10.17	-	-	2 month 19.10.17	-	-	✓	-	-	Few	No	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					A/G ↑
19	M-6797	b/oSaratha	+	O	31/2 Month	D20 19.10.17	-	-	D20 19.10.17	-	-	D20 19.10.17	-	-	✓	_	-	Few	No	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					A/GC ↑
20	M-7146	B/O Mohanasundharam	+	MMC	D 45	POD 15 NG	11/2 y NG	2 Yr 3.11.17	NG	11/2y NG	2 Yrs NG	NG	-	6 Mon NG	✓	_	-	Moderate	No	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					A/GC ↑
21	M-7297	Bhagavan	+	POST TBM	3 yrs	POD 20 NG	4 yrs NG	5 Yrs 10.11.17	NR	NR	Removed and C/s 10.11.17	NR	11/2 Y NG	5Yrs 10.11.17	✓	_	-	Moderate	-	NG AFB Smear negative	LJ Medium NG	NG Scanty	NIL	NG	↓	↑	↑	↑	↑	NG					A/GC ↑
22	M-7339	B/o Kalpana Selvi	+	MMC/MR/Shunt Extrusion	3 month	POD 5 12.9.17 NG	14.11.17	-	POD-5 12.9.17	Shunt Extrusion	-	-	14.11.17	-	✓	_	-	Plenty	Few GPC	White Opaque Colony	White Opaque Colony	White Opaque Colony	Coagulase (P) Mod .OX (P)	NG	↓	↑	↑	↑	↑	CoNS	VAN, AMC,LZ	_	COT, CFS,CIP,AMP AK		22/2/18 pt dlied due to septicemia
23	M-7709	Boopalan	+	POST TBM	5 yrs 1/9/15	10 POD after VPS SURGERY	1/12/16 NG	DOS 28/11/17	Revision done at NG	Surgery MMC	DOS 28/11/17	NG	NG	DOS 28/11/17	✓	-	-	Moderate	-	Lowenstein Jensen Medium No Growth AFB Smear negative			NIL	NG	↓	↑	↑	↑	↑	NG					Shunt Malobstrut 25/5/18- NG
24	M-7732	Ajay Aswanth	+	o	5 month	POD 5	-	-	POD 5		-	POD 5	-	-	✓	_	_	-	-	-	-	-	NIL	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
25	M-8020	Ragavan	+	H -SOL	12/12/2017	DOS 6 POD	REV 1 5.1.18	REV 2 22.2.18	DOSVenticular encl 18/12/17	REV 1 01-05-2018	REV 2 22/2/18	DOS 18-12-2018	REV 1 01-05-2018	REV 2 22/1/18	✓	-	-	Moderate	Gram Negative GNCB Seen	18.12.17 5.1.18 22.2.18 Pale LF/GWC	18.12.17 5.1.18 22.2.18 Pale LF/GWC	18.12.17 5.1.18- No Growth 22.2.18 Pale LF/GWC	Supporting	NG	↓	↑	↑	↑	↑	acinetobacter			NET, MRP,PIT, CIP,COT, AK,G	MBL	22/2/18 pt dlied due to septicemia
	M-83309 22-12-2017	B/o Saranya	+	O	31/2 month	POD 10 day	-	-	POD 10 day	-	-	POD 10 day	-	-	✓	-	_	-	-	-	-	-	NIL	NG	↓	↑	↑	↑	↑	NG					A/GC↑

27	M-7920 22-12-2017	Vaishak	+	O	21/2	POD 5 day	-	-	NO SHUNT SAMPLE			POD 5 day	-	-	✓	_	_	Few Pus	-	-	-	NG	NIL	NG	↓	↑	↑	↑	↑	NG					A/GC↑
28	M-079 04.01.2018	B/O Neelamegam	+	MMC , MR	D40	POD 10 Day NG	2.12.18 NG	4.1.18 Pale of Sample Collector	D50	2.12.18	4.1.18 Date of Sample	D50	2/12/2018	4.1.18 Date of Sample	✓	_	-	Few Pus	Few GNB	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
29	M-100 04.11.18	Bhavani Picu case	+	Post Traumatu hrdrocephe	9Yrs	POD 7 Day	-	-	NO SHUNT SAMPLE			POD 7 Day			_	-	✓	Few Pus	Few GNB	NG	-	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
30	M-102 04.01.2018	B/o Krishnaveni	+	MMC , MR	D40	POD 10 Day NG	2 Month NG	4 Month 4.1.18	-	-	Shunt removed 04.1.18	NG	NG	Current Sample Collection 4.1.18	_	-	✓	Few Pus	Few GPC	White Opaque Colony	White Opaque Colony	White Opaque Colony	Coagulase (P) Mod .OX (P) HUGH LEIFSON oxidative	NG	↓	↑	↑	↑	↑	CoNS	VAN, AMC B-(s), FZ-(R)	_	COT, LZ,CFS,CIP, AMP AK		Alive /GC ↑
31	M-169 07/01/2018	B/o Mehitha	+	MMC , MR	D40	POD 5Day NG	DOS 2/12 Month 7.1.18	-	INTACT	DOS 7.1.18	-	45 Days NG	DOS 7.1.18	-	✓	-	-	Few Pus	Few GPC	White Opaque Colony	White Opaque Colony	White Opaque Colony	Coagulase (P) Mod .OX (P) HUGH LEIFSON oxidative	NG	↓	↑	↑	↑	↑	CoNS	VAN, B-(s), FZ-(R)	-	AMC,COT, LZ,CFS,CIP, AMP AK		Alive /GC ↑ reshinted after 1 wk
32	M-776 31.01.2018	B/o Vedhapriya	+	Preterm IVH	D40	POD 2	-	-	NO SHUNT SAMPLE			31/1/18	-	-	✓	-	-	Many	-	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Dead D42
33	M-796 31-1-2018	B/o Maheswari	+	Preterm IVH	D40	POD 5	-	-	NO SHUNT SAMPLE			31/1/18	-	-	✓	-	-	Many	-	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Dead D50
34	M-1163 14.02.2018	Ashwin	+	O	D30	POD 10 Day NG	2 month 14.2.18	-	-	shunt 14.2.18	-	-	Blood 14/2/18	-	✓	-	-	Many	Few GPC Seen	White Opaque Colony	White Opaque Colony	White Opaque Colony	Coagulase (P) Mod .OX (P) HUGH LEIFSON oxidative	NG	↓	↑	↑	↑	↑	CoNS	VAN, B-(s), FZ-(R)	-	AMC,COT, LZ,CFS,CIP, AMP AK		Alive /GC ↑
35	M-1236 17.02.2018	B/o Saranya kannan	+	Preterm IVH	3 month	15 Days after surg 17.2.18	-	-	Shunt 17.2.18	-	-	Blood 17.2.18	-	-	✓	-	-	Few	NO	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG	-	-			Alive /GC ↑
36	M-1549 28.02.2018	B/o Sakitha	+	PRETERM	D35	POD 2 28/2	-	-	Shunt 28/2	-	-	Blood 28/2	-	-	✓	-	-	Many	Few GPC in Cluster	White Opaque Colony	White Opaque Colony	White Opaque Colony	Coagulase (P) Mod .OX (N) HUGH LEIFSON fermentative	NG	↓	↑	↑	↑	↑	staph aureus	VAN, B-(R), FZ-(S)		AMC,COT, LZ,CFS,CIP, AMP AK		Dead 2 POD
37	M-1633 03.03.2018	Lakshmi Krishnan	+	POST TRAUMATC HYDROCEP	7yrs	10th POD 3.3.18	-	-	-	-	-	Blood 3.3.18	-	-	✓	-	-	Many	No	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
38	M-1814 10.3.2018	Raghhasudha Trauma ward	+	Post Traumatu hrdrocephe	91/2 yrs	15th POD 10.3.18	-	-	Shunt 10.3.18	-	-	Blood 10.3.18	-	-	✓	-	-	Many Pus	No	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Dead
39	M-1824 10.3.2018	B/o valli	+	O	21/2 Months	15th POD 10.3.18	-	-	Shunt 10.3.18	-	-	Blood 10.3.18	-	-	✓	-	-	Few	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
40	M-1825 10.3.2018	B/o Deepa	+	O	2 month	5th POD 10.3.18	-	no shunt sample				Blood 10.3.18	-	-	✓	-	-	Few	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
41	M-1967 15.3.18	Sunil Kumari	+	H-SOL astrocyloma	7.1.18 SOL Excis 28.2.18 VP Shunt Inse	D17 Infection 15/3/18	-	-	D17 15.3.18	-	-	D17 15.3.18	-	-	✓	-	-	✓	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
42	M-2007 17.3.18	Jais Ni	+	Sporadic Hydrocephe tes	13/4 age 7.1.18	2 month 17..18	-	no shunt sample			-	17.3.18	-	-	✓	-	-	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
43	M-2627 17.3.18	B/o Abimanya	+	O	2 month	20th POD 17.3.18	-	-	POD 20 17.3.18	-	-	POD 20 17.3.18	-	-	✓	-	-	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
44	M-2780 23.3.18	B/o Kavi Mozhi	+	O	3 month	10th POD 23.3.18	9/5/18 M-3259	no shunt sample				23.3.18	9/5/18 M-3059	-	✓	-	-	-	✓	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
45	M-2627 11.4.18	Aishwarya	+	O	10 month 19.2.18	After 2 month 11.4.18	-	-	No Shunt Sample			19.2.18	-	-	✓	-	-	✓	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
46	M-3340 13.5.18	B/o Saranya	+	MMC, MR	2 month	15th POD 13.5.18 NG	8/7/2018	-	13.5.18	8/7/2018	-	13.5.18	8/7/2018	-	✓	-	-	-	✓	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					
47	M-4025 9.6.18	B/o Revathi	+	MMC, MR	21/2 Months	15th POD 9.6.18	10/8/2018	-	POD 15 9.6.18	10/8/2018	-	POD 15 9.6.18	10/8/2018	-	✓	-	-	-	✓	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					
48	M-4308 12.6.18	Sumardha	+	H-SOL	1 month Prior SOL removed VP Shunt Intrusion	18th POD 20.6.18	-	-	POD 18.20.6.18	-	-	13.5.18	-	-	✓	-	-	FEW	FEW GPC CLUSTER S	White Opaque Colony	White Opaque Colony	White Opaque Colony	Coagulase (P) Mod .OX (P) HUGH LEIFSON oxidative	NG	↓	↑	↑	↑	↑	CoNS	VAN, B-(s), FZ-(R)	-	AMC,COT, LZ,CFS,CIP, AMP AK		Alive /GC ↑
49	M-4310 12.6.18	Balaji	+	H-SOL Astrocycle	1 month Prior SOL removed VP Shunt Intrusion	20th POD 20.6.18	DOS 2/12 Month 7.1.18	✓	POD 20 20.6.18	-	-	POD 20 20.6.18	-	_		L_	-	-	-	NG	NG	NG		NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
50	M-4435 12.6.18	Dyan Yadhan	+	MMC, MR	D40	D15 25.6.18	-	-	25.6.18	-	-	25.6.18	-	-	✓	_	-	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Alive /GC ↑
51	M-5201 18.6.18	B/o Masilamani	+	P	D40	D5 25.6.18	-	-	D5 25.6.18	-	-	D5 25.6.18	-	-	✓	__	_	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Dead
52	M-6054 18.6.18	Angel	+	Sporatic H	5 month/ FCH	9 months 29.6.18	✓	✓	9 months 29.6.18	-	-	9 months 29.6.18	-	_		L	_	FEW	FEW GNB	NLF/GWC	NLF/GWC	NLF/GWC	OX &Citrate (P) TSI - K/NC	NG	↓	↑	↑	↑	↑	pseudomonas	MRP,PIT, CFS	Amp,CIP,LE,AK,G			2.7.18 pt died due to septicemia
53	M-6056 18.6.18	Aswini Pandi	+	P	D40	10th POD 29.6.18	10thPOD 29.6.18	✓	10th POD 29.6.18	-	-	10th POD 29.6.18	-	_	✓	-	-	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					Dead
54	22.6.18	Akilesh	+	O	5 yrs			✓			✓			✓	✓	-	-	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					AliveGC ↑
55	26.6.18	B/o. Selvamani	+	O	3 months	15th POD		15th POD			15th POD					L	-	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					AliveGC ↑
56	26.6.18	Sushmitha	+	Sporatic H	1month before	30th POD	-	-	30th pod	-	-	30th POD	-	-	✓	-	-	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					AliveGC ↑
57	29.6.18	Subiksha	+	Sporatic H	AT 10 month	30 th POD	_	(-)	30th pod	-	_	30th POD	_	_	✓	-	_	-	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					AliveGC ↑
58	29.6.18	Dhanashree	+	Post TBM	AT 8 month	40th POD	✓	-	40th POD	✓	-	2 month	_	_	-	-	✓	Few	-	NG	NG	NG	-	NG	↓	↑	↑	↑	↑	NG					AliveGC ↑
59	29.6.18	Praneeth	+	O	4mon Obst Hydro	6mon 06/06/17	-	-	6mon 06/06/17	-	-	6mon 06/06/17	_	-	-	-	✓	-	Few GNB	NG	NG	NG	NIL	NG	↓	↑	↑	N	↑	NG					Alive GC↑
60	29.6.18	B/O Deivani	+	P	D35	5TH POD 06/06/17	-	-	5th POD 6/6/17	-	-	5th POD 6/6/17	-	-	-	-	✓	Few	-	NG	NG	NG	NIL	NG	↓	↑	↑	↑	↑	NG					Alive GC↑

DOS: Date of Surgery
REV: Revision

MMC,MR: Myelomeningocele with multiple revisions
SOL-H: Space occupying lesions followed by hydrocephalus

P: Pre term with Intraventricular haemorrhage
O: Obstructive hydrocephalus

CoNS:
POD: